REPORT OF
THE NATIONAL INSTITUTES OF HEALTH
AD HOC WORKING GROUP
TO DEVELOP
RADIOEPIDEMIOLOGICAL TABLES

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service   National Institutes of Health

REPORT OF THE NATIONAL INSTITUTES OF HEALTH

AD HOC WORKING GROUP TO DEVELOP RADIOEPIDEMIOLOGICAL TABLES

Responding to the Congressional Mandate under Section 7(b) of the

Orphan Drug Act of January 4, 1983 (PL 97-414)

January 4, 1985

Published by the
Office of the Director
National Institutes of Health

NIH Publication No. 85-2748

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service   National Institutes of Health

AD HOC WORKING GROUP TO DEVELOP RADIOEPIDEMIOLOGICAL TABLES

ROSTER OF MEMBERS

J. Edward Rall (Chairman)
Deputy Director for Intramural Research
National Institutes of Health
Shannon Building, Room 122
Bethesda, Maryland 20205
(301) 496-1921

Gilbert W. Beebe
Clinical Epidemiology Branch
National Cancer Institute
Landow Building, Room 8C41
Bethesda, Maryland 20205
(301) 496-5067

David G. Hoel*
Director of Biometry and
  Risk Assessment Program
National Institute of Environmental
  and Health Sciences
PO Box 12233
Research Triangle Park, NC 27709
(919) 541-3441 (FTS 8-629-3441)

Seymour Jablon
National Research Council
2101 Constitution Avenue
Washington, D.C. 20418
(202) 334-2825

Charles E. Land
Radiation Epidemiology Branch
National Cancer Institute
Landow Building, Room 3A22
Bethesda, Maryland 20205
(301) 496-6600

Oddvar F. Nygaard, Director
Division of Radiation Biolo..
Department of Radiology
Case Western Reserve University
2058 Abington Road
Cleveland, Ohio ...106
(216) 844-3539

Arthur C. Upton
Professor and Chairman
Department of Environmental Medicine
New York University Medical Center
550 First Avenue
New York, NY 10016
(212) 340-5280

Rosalyn S. Yalow
Senior Medical Investigator
Veterans Administration Medical Center
130 West Kingsbridge Road
Bronx, NY 10468
(212) 579-1644

Victor H. Zeve (Executive Secretary)
Special Assistant
Office of the Director
National Cancer Institute
Building 31, Room 4B47
Bethesda, MD 20205
(301) 496-5854

*Address during 1983-84:
 Board of Directors
 Radiation Effects Research Foundation
 2-5 Hijiyama Park, Minami-ku
 Hiroshima-shi, 730
 Japan

TABLE OF CONTENTS

EXECUTIVE SUMMARY

Public Law 97-414, the Orphan Drug Act, passed by the Congress and
enacted on January 4, 1983, directed the Secretary of Health and Human
Services to construct radioepidemiological tables showing the probability
that certain cancers could result from prior exposure to radiation.

To ensure as far as possible that the radioepidemiological tables
would represent the best possible scientific judgment, the Secretary of
Health and Human Services established the NIH Ad Hoc Working Group to
Develop Radioepidemiological Tables. To assist the Working Group, the
NIH and the Assistant Secretary for Health requested the National Academy
of Sciences to form an advisory committee (the National Academy of Sciences
Oversight Committee on Radioepidemiologic Tables). The Working Group would
like to thank Dr. C. Frederick Mosteller and the other members of the
Oversight Committee for their constructive criticisms, which have been of
great benefit during the preparation of the report. The Working Group
also benefited greatly from the groundwork laid by the National Council
on Radiation Protection and Measurements (NCRP) Committee No. 71, which
already was addressing the question of probability of causation (PC) for
radiogenic cancers. Finally, the Working Group has had an opportunity to
interact with the Science Panel of the Committee on Interagency Radiation
Research and Policy Coordination, Office of Science and Technology Policy,
Executive Office of the President, during the course of the Panel's
evaluation of the tables, and has its report dated November, 1984.

In constructing the tables, the NIH Working Group and the Oversight
Committee identified the same set of problems involved in the calculation
of probability of causation for cancer following exposure to ionizing
radiation. Additionally, the Oversight Committee has made several important
suggestions that a future committee, whose task is to update this report,
should find useful.

The Working Group determined that it could not attempt a new analysis
of the epidemiologic data but should base many of its calculations on the
report issued in 1980 by the National Academy of Sciences Committee on the
Biological Effects of Ionizing Radiation (BEIR III) (1) that itself had
required more than three years to complete. The Working Group, however,
did depart from the BEIR III report in several important details because
of the availability of new data. These include adoption of a new "wave
function" time-response model for leukemia and bone cancer, different co-
efficients for leukemia and cancers of the lung, thyroid and breast,
addition of cancer of the salivary gland, omission of lymphoma as a
radiation-induced cancer, and avoidance of PC calculations for certain
cancers following exposure at younger ages. Overall, of the 78 age-,
sex-, and site-specific risk coefficients employed in the present report,
40 were taken directly from the BEIR III report and 38 were obtained from
more recent sources.

The problems recognized by both groups can be resolved more accurately
in the future through the accumulation of more human data, and especially
by new insights into the mechanisms of carcinogenesis, and perhaps, rather
less by mathematical ingenuity or further in-depth analysis of existing

data, although more refined analysis of newer data will be useful. The Working Group interpreted its mandate from the Orphan Drug Act as requiring assessment of currently available data and the exercise of its best judgment regarding the handling of the scientific uncertainties that are at present unresolved.

Historically, not long after ionizing radiation was discovered in 1895 and methods for producing and utilizing various types of radiation became available, it was demonstrated that such radiation could be seriously damaging. First came the recognition that radiation to the skin could cause a serious, sunburnlike effect. By 1904 it was learned that radiation could cause skin cancers, and somewhat later (1911) it was shown that the incidence of leukemia was elevated in radiologists.

In 1928 the International Congress of Radiology adopted the first international recommendation for radiation protection. At that time, it was believed that there was a threshold for the deleterious effects of radiation, that is, a dose below which there would be no damage. Work on the genetic effects of radiation in the 1930's suggested that any dose of radiation had a certain likelihood of producing a damaging effect on germ cells. Concern over the genetic effects of radiation (2), so prevalent in the 1950's, has lessened in the last two decades, whereas the carcinogenic effects of radiation have become much more evident.

Radiation acts to cause cancers in a largely random manner. In a situation in which a large number of people have received a moderate-to-large amount of radiation, the numbers of cancers of specific sites (e.g., breast cancer, leukemia, etc.) produced by that amount of radiation can be estimated. We cannot, however, predict which individuals will develop cancer. Even after the cancer has developed, we cannot state with certainty whether it was caused by radiation, since it is usually impossible to differentiate cancers induced by irradiation from those which occur "normally" in the population.

Cancers appear to be associated with a large number of environmental factors and genetic susceptibilities although, in any individual case, it is usually not possible to be sure of the exact cause of the cancer. The events that may cause or predispose to cancer interact in several ways, but only a few of these interactions are known and understood. Moreover, different individuals are exposed differently, and to a greater or lesser extent, to various carcinogenic factors as the result of cigarette smoking, alcohol consumption, viral infection, dietary habits, occupation, heredity, etc. If detailed knowledge were available about the effects of all these exposures and interactions, it would be possible theoretically to classify individuals into a large number of groups among which the probability of causation of a particular cancer by a given agent could be calculated more accurately. For any carcinogen, however, including radiation, the number of such groups is severely limited at present; i.e., from available data we can, with some assurance, partition populations into categories based only on a few factors, including age at diagnosis, sex, smoking history and age at exposure to radiation. Except for these subdivisions we calculate probabilities of causation only for aggregate groups in which unknown variations among individuals may be appreciable. However, probabilities of causation based on even the most minimal partitioning are valid probabilities for these groups.

Attempts to estimate the probability that an observed effect resulted from one of several possible causes are not uncommon, even in the more exact physical sciences. Decay of short-lived subatomic particles, where only a small number of events can be observed and several potential mechanisms exist, is in some respects analogous to the problems involved in constructing radioepidemiological tables. In both cases, probabilities are calculated from a small number of events. There is, however, an important difference. In physics a large number of well-tested and comprehensive theories exists to guide calculations, whereas in biology and medicine there are few well-established general and predictive theories and the systems are immeasurably more complex. This becomes particularly important for calculation of the probability that radiation caused a certain cancer when the dose of radiation was small. Such calculations are therefore subject to great uncertainty (see Chapter VII).

In order to construct the radioepidemiological tables, several fundamental decisions were made, which are explained in the remainder of this Summary.

I. The Working Group first had to decide what data should be used to develop the numbers in the tables. In general, epidemiologic data derived from radiation exposure to humans were utilized. However, effects in experimental animals, largely rodents, and additional data from in vitro studies of effects of radiation on cell cultures, which can provide useful information on principles, were also considered. The animal data on low levels of ionizing radiation are constrained by the same limitations as the data on humans--the difficulty that the small effects require very large numbers of animals. Furthermore, the studies on rodents have been restricted almost entirely to highly inbred strains of animals and to types of tumors that occur with high frequency. Hence their relevance to the carcinogenic effects of low-level irradiation in the human population is uncertain. The in vitro experiments suffer because the cells are studied under conditions that differ profoundly from those in vivo, and are of uncertain relevance to the carcinogenic effects of irradiation in man (3).

II. Secondly, the Working Group had to resolve how to estimate the risks from low doses of radiation. Although effects of moderate-to-high doses on large populations can be estimated reasonably well, several government reports, such as the 1979 Report of the Work Group on Science of the Interagency Task Force on the Health Effects of Ionizing Radiation (4), the 1981 report of the Comptroller General to the U.S. Congress (5), and the 1981 report of the Interagency Radiation Research Committee (6), as well as such authoritative reports as the 1980 (BEIR III) report of the National Academy of Sciences (1) and the 1977 report of the United Nations Scientific Committee on the Effects of Atomic Radiation (7), testify to the uncertainty of the carcinogenic effects of very low doses of radiation. Thus, the BEIR III committee was unwilling to make estimates of the carcinogenic effects of radiation for acute doses below 10 rad or for continuing exposure to doses below 1 rad per year. Although the non-threshold hypothesis is accepted for radiation protection purposes, empirical evidence as to the existence of a threshold is lacking.

Some environmental and occupational doses are quite small, on the order of those resulting from natural background radiation to which we are all exposed (about 0.08 to 0.2 rem per year in the United States). It might be supposed, therefore, that studies of populations living in regions where background levels vary greatly would yield estimates of carcinogenic risks associated with such differences. Several such studies have been attempted, but the risks are so low that any effect of variation in background radiation is overshadowed by the natural variations in cancer incidence (1,7-9). At the present time, estimations of effects at low doses are based upon assumptions as to the mathematical form governing the dependence of effect upon dose, since we must extrapolate from the dose region where we have evidence of effects, to lower doses where effects have not been observed or may not be large enough to be detectible.

In general, the Working Group has sought to use the dose-effect model for each cancer which is most consistent with both the human epidemiologic data and the radiobiological data. For leukemia, the data are consistent with a so-called linear-quadratic model; hence this model is the basis for the PC tables calculated for leukemia. This model utilizes two constants and, in general, predicts that small doses of radiation have a lesser effect per rad than do higher doses. There are radiobiological reasons for assuming that a linear-quadratic dose-effect model is generally applicable to other cancers, which are discussed both in the BEIR III report and in Chapter III of the present report. Accordingly, we have used this approach for all cancers except those of the thyroid and breast. For carcinoma of the breast and thyroid, the data appear to be best described by a simple linear relationship in which the carcinogenic effect of radiation is directly proportional to the dose; again, the tables are based on this interpretation.

III. The Working Group also had to consider the relative effectiveness of radiation delivered at different dose rates. Although there are no conclusive human data on the carcinogenic effect of radiation delivered at a very low dose rate relative to that delivered at a high dose rate (atom bomb survivors, therapeutic radiation), several national and international bodies have suggested that radiation of low linear energy transfer (low LET) is considerably less carcinogenic at a low dose rate than at a high dose rate (6,7,10). If a linear-quadratic model is used, no separate dose-rate correction is necessary for protracted radiation exposures, given a certain partitioning of the dose (see Chapters III-I and V-B). In the case of carcinoma of the breast and thyroid, the use of the linear dose-effect model implies that there should be no dose-rate effect; data available for both of these cancers are consistent with this prediction.

IV. An additional assumption required for calculation of PC values concerns the relationship between the number of cancers produced at any given time after radiation and the number normally occurring in a similar population of the same age and sex not exposed to radiation. The BEIR III report utilized both a relative risk time projection model and an absolute risk time-independent model. The absolute risk model assumes that the radiation-induced risk of developing cancer is constant after a suitable latent period following irradiation. The relative risk time projection model states that, at any time after a latent period, a given

dose of radiation increases the probability of developing cancer by a constant fraction of the baseline risk. Available data, particularly on breast and lung cancer in Japanese atomic bomb survivors, which have appeared since the preparation of the BEIR III report, support the relative risk time-projection model more convincingly. Therefore, the Ad Hoc Group has adopted this model, as discussed in Chapter III.

There is a substantial body of data on the risk of developing leukemia (both acute leukemia and chronic granulocytic leukemia) after radiation. Hence, it is possible to dvelop a model that accurately follows the observed data. This model is basically wave-like in form, following neither the constant absolute risk nor the constant relative risk time-projection model. Accordingly, we have used the wave-like model to describe the risk of developing leukemia as a function of time after radiation.

V. A problem awaiting resolution is the relative carcinogenicity of high-LET radiation. This is the type of radiation delivered by large, highly energetic particles such as neutrons or alpha particles. For the same absorbed dose this kind of radiation appears to be more effective in causing cancers than low-LET radiation, such as that delivered by X rays or gamma rays. All the tables except for bone cancer, and for lung cancer after exposure to radon (which occurs principally in uranium miners), deal with the more commonly occurring low-LET radiation. Several committees are currently investigating the carcinogenic effects of high-LET radiation. Pending their conclusions, it is not possible to use these tables relevant to low-LET radiation for the calculation of PC estimates for high-LET radiation unless a biologically equivalent dose can be determined for the individual case.

Other estimates of probability of causation, or their equivalent, have been prepared by British Nuclear Fuels, Limited (BNFL), by Gofman (11), and by Stewart (12). The BNFL procedure is not available to the public, and certain objections have been raised to the Gofman calculations (13). Stewart's analysis was based on data from the Hanford workers (14), which are much too limited to provide any basis for a compensation system (15,16). The present report represents a consensus of the Working Group, aided by its interaction with the Oversight Committee of the National Academy of Sciences and the Science Panel of the Committee on Interagency Radiation Research and Policy Coordination.

Chapter I of the report outlines the Congressional actions that mandated its preparation; Chapter II describes briefly what is known about human cancer. Chapter III describes relations between radiation and cancer, including a listing of those cancers which may be caused by radiation and for which adequate data are available to calculate PC, and those for which an association with radiation is not proved. Chapter IV describes concepts involved in calculating the probability that any given amount of radiation was the cause of any particular cancer. Chapter V lists data sources and assumptions that are required for calculations of PC values and justifies these choices. Chapter VI describes how the calculations have been performed. Uncertainties in the basic data and assumptions which are necessary ingredients in the calculation of probabilities of causation are reflected in uncertainties in the final PC values themselves. An attempt has been made in Chapter VII to identify

and assess the various sources of uncertainty and to combine these uncertainties into single measures for individual cancers. The combined uncertainties, while not small, are not so large as to negate the usefulness of the PC's, especially at the low and high ends of the scale. Chapter VIII discusses how the present PC estimates may be updated and describes what new information may become available, and how it might be handled. Chapter IX describes how to calculate the probability of causation for any radiation dose and any cancer using only a few tables, which appear in Chapter X. In Chapter X each cancer for which a probability of causation can be calculated is discussed and specific examples of calculations are presented, together with tables of the constants necessary for these calculations. This arrangement has necessarily given rise to some redundancy, but the Working Group believes that the present format permits anyone to obtain all the basic information for calculation of PC for a specific cancer in any specific case from just one of the subsections of Chapter X.

In Appendix I, tables of the probability of causation for individual cancers are presented for radiation doses of 1, 10 and 100 rad. For any specific case, the reader is encouraged to use the simple formulae in Chapter X for calculation of a probability of causation.

In Appendix II, the Working Group has reproduced the specific recommendations of the NAS Oversight Committee with respect to the July, 1984 draft of the present report and its future revisions (17). Since this final version of the Tables incorporates most of the recommendations made by the Oversight Committee, each recommendation is annotated as to its status in the final report presented here.

Appendix III is a glossary of some of the terms used in this report.

J. E. Rall, M.D., Ph.D., Chairman,
NIH Ad Hoc Working Group to Develop
Radioepidemiological Tables

January 4, 1985

REFERENCES - Executive Summary

1. Committee on the Biological Effects of Ionizing Radiation, "The Effects on Populations of Exposure to Low Levels of Ionizing Radiation: 1980." National Academy Press, Washington, D.C., 1980.

2. NCRP Report no. 17. "Permissible Dose from External Sources of Ionizing Radiation", National Bureau of Standards Handbook No. 59, issued September 24, 1954.

3. Borek, C., Radiation Oncogenesis in Cell Culture. Adv. Cancer Res. 37: 159-232 (1982).

4. "Report of the Interagency Task Force on the Health Effects of Ionizing Radiation. Work Group on Science." U.S. Department of Health, Education and Welfare, Washington, D.C., June 1980.

5. Comptroller General, "Report to the Congress of the United States, January 2, 1981 (EMD-81-1): 'Problems in Assessing the Cancer Risks of Low-Level Ionizing Radiation.'" Accounting Office, Document Handling and Information Handling Facility, P.O. Box 6015, Gaithersburg, MD 20760.

6. Interagency Radiation Research Committee, "Federal Strategy for Research into the Biological Effects of Ionizing Radiation" (NIH Publication No. 81-2407). U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, June 1981.

7. United Nations Scientific Committee on the Effects of Atomic Radiation, "Sources and Effects of Ionizing Radiation." United Nations, New York, 1977.

8. Land, C. E., Estimating Cancer Risks from Low Doses of Ionizing Radiation. Science 209: 1197-1202 (1980).

9. High Background Radiation Research Group, China. Health survey in high background radiation areas in China. Science 209: 877-880 (1980).

10. NCRP Report No. 64. "Influence of Dose and Its Distribution in Time on Dose-response Relationships for low-LET Radiations." National Council on Radiation Protection and Measurements, Washington, D.C., 1980.

11. Gofman, J. W., "Radiation and Human Health." Sierra Club Books, San Francisco, 1981.

12. Stewart, A. M., Health Risks of Low Level Radiation - A Guide to the Use of MSK Risk Estimates for Radiation Workers. (Presented by Dr. Stewart at a meeting in Philadelphia, PA, December, 1982.)

13. Orient, J. M., A Critique of the Statistical Methodology in Radiation in Human Health, John W. Gofman. Health Phys. 45: 823-824 (1983).

14. Mancuso, T. F., Stewart, A., and Kneale, G., Radiation Exposures of Hanford Workers Dying from Cancer and Other Causes. Health Phys. 33: 369-385 (1977).

15. Anderson, T. W., Radiation Exposures of Hanford Workers: A critique of the Mancuso, Stewart and Kneale report. Health Phys. 35: 743-750 (1978).

16. Hutchison, G. B., MacMahon, B., Jablon, S. and Land, C. E., Review of a Report by Mancuso, Stewart and Kneale of Radiation Exposure of Hanford Workers. Health Phys. 37: 207-220 (1979).

17. Oversight Committee on Radioepidemiological Tables, "Assigned Share for Radiation as a Cause of Cancer - Review of Radioepidemiological Tables Assigning Probabilities of Causation" (Final Report). National Academy Press, Washington, D.C., 1984.

Chapter I: LEGISLATIVE AUTHORITY

A. Background

On January 4, 1983 the President of the United States signed Public
Law 97-414 (known as the "Orphan Drug Act"), an act to amend the Federal
Food, Drug and Cosmetic Act to facilitate the development of drugs for
rare diseases and conditions, and for other purposes. This legislation
includes a provision (Section 7 (b) of the bill) directing the Secretary
of Health and Human Services to "devise and publish radioepidemiological
tables that estimate the likelihood that persons who have or have had any
of the radiation-related cancers and who have received specific doses
prior to the onset of such disease developed cancer as a result of these
doses." The complete text of section 7 (b) of the bill and an excerpt
from President Reagan's statement, on the occasion of his signing the
Orphan Drug Act, are included in section B of this chapter.

On February 25, Dr. Edward N. Brandt, Jr., Assistant Secretary for
Health, Department of Health and Human Services, assigned lead respons-
ibility for the implementation of this charge to the National Institutes
of Health. An Ad Hoc Working Group, chaired by Dr. J. E. Rall, Deputy
Director for Intramural Research, NIH, was established; this group has
met regularly since April 5, 1983. Subsequently (August 4, 1983), the
Secretary of Health and Human Services approved the Charter for an "Ad
Hoc Working Group to Develop Radioepidemiological Tables" to carry out
this mandate. The text of the Charter is included as section C.

It may be noted that the section of P.L. 97-414 pertaining to the
development of radioepidemiological tables originally was introduced by
Senator Orrin Hatch (Utah) as a part of Senate bill S 1483: "Radiation
Exposure Compensation Act" to provide for damages due to radiation exposure
from nuclear weapons tests in Nevada. Since neither this bill nor the
companion House bill (H.R. 6052) was reported out of the respective
committees, the section relating to radioepidemiological tables was
attached as an amendment to the "Orphan Drug Act" which was passed by
both houses and signed into law on January 4, 1983. On March 23, 1983,
Senator Hatch introduced the "Radiogenic Cancer Compensation Act" which
intends to use as the basis for award of compensation the tables of
probability of causation of cancer from radiation exposures, prepared in
response to the requirements of the "Orphan Drug Act."

B. Public Law 97-414 - January 4, 1983

"7(b)(1) Within one year after the date of enactment of this Act, the
Secretary of Health and Human Services shall devise and publish radio-
epidemiological tables that estimate the likelihood that persons who have
or have had any of the radiation-related cancers and who have received
specific doses prior to the onset of such disease developed cancer as a
result of these doses. These tables shall show a probability of causation
of developing each radiation related cancer associated with receipt of
doses ranging from 1 millirad to 1,000 rads in terms of sex, age at time
of exposure, time from exposure to the onset of the cancer in question,

and such other categories as the Secretary, after consulting with appropriate scientific experts, determines to be relevant. Each probability of causation shall be calculated and displayed as a single percentage figure.

(2) At the time the Secretary of Health and Human Services publishes the tables pursuant to paragaph (1), such Secretary shall also publish—

(A) for the tables of each radiation related cancer, an evaluation which will assess the credibility, validity, and degree of certainty associated with such tables; and

(B) a compilation of the formulas that yielded the probabilities of causation listed in such tables. Such formulas shall be published in such a manner and together with information necessary to determine the probability of causation of any individual who has or has had a radiation related cancer and has received any given dose.

(3) The tables specified in paragraph (1) and the formulas specified in paragraph (2) shall be devised from the best available data that are most applicable to the United States, and shall be devised in accordance with the best available scientific procedures and expertise. The Secretary of Health and Human Services shall update these tables and formulas every four years, or whenever he deems it necessary to insure that they continue to represent the best available scientific data and expertise."

Excerpt from President Reagan's statement on the occasion of his signing the Orphan Drug Act

". . . there is as yet no consensus among radiation experts in relating human cancers and exposure to low levels of radiation. Yet, Section 7 mandates that probability of causation tables be calculated for even very small dose levels. Accordingly, I am directing the Secretary of Health and Human Services to complete the tables to the extent that may be possible and scientifically responsible, in light of the analysis also mandated by Section 7, which requires him to 'assess the credibility, validity, and degree of uncertainty associated with such tables.'"

C. Charter – Ad Hoc Working Group to Develop Radioepidemiological Tables

"Purpose

Section 7(b) of Public Law 97-414 directs the Secretary of Health and Human Services to devise and publish radioepidemiological tables that estimate the likelihood that persons with any radiation-related cancer who received specific radiation doses before the onset of the cancer developed the disease as a result of such exposure. The tables must show the probability of causation for each cancer associated with receipt of doses ranging from 1 millirad to 1,000 rads in terms of sex, age at time

of exposure, time from exposure to disease onset, and such other categories as the Secretary, after consultation with appropriate scientific experts, determines to be relevant.

In carrying out this mandate, the Secretary deems it necessary to establish an Ad Hoc Working Group to Develop Radioepidemiological Tables comprised of scientific experts whose qualifications will insure a thorough, competent, and timely completion of the task.

"Authority

42 U.S. Code 217a, Section 222 of the Public Health Service Act, as amended.

This Ad Hoc Working Group to Develop Radioepidemiological Tables is governed by the provisions of Public Law 902-463, which sets forth standards for the formation and use of advisory committees.

"Function

In addition to developing radioepidemiological tables, the Ad Hoc Working Group shall:

1. Assess the credibility, validity, and degree of certainty associated with such tables; and

2. Compile the formulas that yielded the probabilities of causation listed in such tables. Such formulas shall be published in such a manner and together with information necessary to determine the probability of causation of any individual who has or has had a radiation-related cancer and has received any given dose.

The tables specified in pargaraph (1) and the formulas specified in paragraph (2) shall be devised from the best available data that are most applicable to the United States, and shall be devised in accordance with the best available scientific procedures and expertise. The Secretary of Health and Human Services shall update these tables and formulas every four years, or whenever necessary, to insure that they continue to represent the best available scientific data and expertise.

"Structure

The Ad Hoc Working Group to Develop Radioepidemiological Tables shall consist of eight members, including the chairperson. Members and chairperson shall be selected by the Secretary, or designee, from outstanding authorities in the fields of endocrinology, radiation biology and pathology, radioepidemiology, biostatistics, and radiobiology. Members shall be invited to serve for a period of one year. Management and support services shall be provided by the Office of the Director, National Institutes of Health.

"Meetings

Approximately eight meetings shall be held at the call of the chairperson who shall also approve the agenda. A government official shall be present

at all meetings. Meetings shall be conducted and records of proceedings
kept as required by applicable laws and Department regulations. Meetings
shall be open to the public, except as determined otherwise by the Secretary;
notice of all meetings shall be given to the public.

"Compensation

Members who are not full-time Federal employees shall be paid at the rate ·
of $100 per day, plus per-diem and travel expenses in accordance with
Standard Government Travel Regulations.

"Annual Cost Estimate

Estimated annual cost for operating the Ad Hoc Working Group, including
compensation and travel expenses for members but excluding staff support,
is $36,700. Estimated annual man years of staff support required is one
at an estimated annual cost of $49,213.

"Reports

Section 7(b) of Public Law 97-414 directs that within one year after the
date of enactment of this Act (January 4, 1983), the Secretary of Health
and Human Services shall publish the radioepidemiological tables. The Ad
Hoc Working Group will complete its task as outlined in the Function
section of this document and submit these findings to the Director,
National Institutes of Health, by October 15, 1983.

"Termination Date

Unless renewed by appropriate action prior to its expiration, the Ad Hoc
Working Group to Develop Radioepidemiological Tables will terminate on
May 15, 1984.

Approved:

    8-4-83   (signed) Margaret M. Heckler "
    ─────────   ──────────────────────────────
     Date   Secretary

- 4 -

Chapter II: THE ETIOLOGY OF CANCER

A. Introduction

Cancer is the second leading cause of death in the United States and has recently become one of the most intensively studied of diseases. Many forms of human cancer are now recognized to have multiple causes. In addition, a number of theories have been proposed to explain the biological mechanisms of carcinogenesis. While our understanding of such mechanisms is still very limited, it is apparent that the overall incidence of cancer is related in large measure to cancer-causing factors in the "environment" defined broadly to encompass air, water, food, and such other factors as individual lifestyle, occupation, smoking habits, sexual activity, etc.

This chapter surveys briefly some of the current theories of cancer. It also summarizes what is known about the more important risk factors that determine the likelihood of cancer in an individual.

B. Current Theories of Carcinogenesis

For many carcinogens the process of tumor development is postulated to involve successive phases, three of which have traditionally been designated the initiation phase, the promotion phase, and the progression phase. During the initiation phase, the DNA of the target cell, which contains the genetic code, is presumed to be damaged or structurally altered as the result of exposure to radiation, a carcinogenic chemical, or some other initiating agent. A variety of molecular mechanisms has been hypothesized to explain the alteration of cellular DNA, including random point mutation, gene rearrangement, chromosomal translocation, and altered DNA methylation (1,2).

The promotional phase of cancer development is concerned with the subsequent changes in the initiated cell that lead to development of an overt tumor. It differs from initiation in a number of respects, being a much slower process, which may cover a major portion of the human lifespan. While a single exposure to an initiating substance can suffice to alter DNA, promoting effects typically are induced only by prolonged contact with the agent in question (2). Promotion may thus be based on different mechanisms; for example, interference with normal regulation of cell growth or with the body's natural defense mechanisms, including repair of DNA damage, conjugation and detoxification of toxicants, immunological resistance, hormone balance, etc. The progressive phase involves the outgrowth of progressively more malignant variants of the original neoplasm.

Together, the promotion and progression of neoplasia are envisioned to involve a series of changes in the regulation of cell growth, with variations in the malignancy of the resulting tumors by the time they become detectable clinically. Some forms of cancer, for example, are known to grow rapidly and metastasize early, while others grow slowly and remain localized indefinitely. These differences, which remain to be fully explained, affect the probability of ascertainment of the cancers in question.

Although much of the research on carcinogenesis has been focused on the initiation phase, promotion may ultimately be of greater importance in determining the incidence of cancer (3). It is noteworthy moreover, that the distinction between initiating and promoting agents is not always clear-cut (2). Radiation and certain chemicals appear to be capable of acting both as initiators and promoters; i.e., as complete carcinogens (4).

Genetic effects leading to cancer may involve germ cells as well as somatic cells. Evidence for the influence of germ cell mutations on human carcinogenesis comes primarily from studies of single-gene defects associated with cancer, family aggregations of neoplasia, and cytogenetic studies showing some cancers to be associated with inherited chromosomal abnormalities. Every form of cancer probably has a heritable component of some magnitude. For some forms it can be large.

It is difficult to estimate the carcinogenic risks of radiation by extrapolation without further knowledge of the precise mechanisms involved in radiation carcinogenesis. Advances in the molecular biology of cancer should eventually lead to new understanding of how radiation induces malignancy and to refinement in our approaches to risk assessment. Significant advances in cancer biology have already come from studies of the genes involved in malignant transformation, some of which are called "oncogenes" (5). Oncogenes discovered originally in tumor viruses have since been found to have homologues in normal cells (6), where they can be "activated" to produce malignant transformation by (a) linking them to powerful retroviral promoters, (b) mutations which may be produced by chemical carcinogens like nitrosomethylurea (7,8), or (c) chromosomal translocations (6-9). Since ionizing radiation is known to cause both point mutations and chromosomal aberrations, it is conceivable that radiation carcinogenesis may, in some instances at least, involve activation of cellular oncogenes. Recently, direct evidence for activation of the c-K-ras oncogene by gamma radiation, through a single base mutation, has been reported (10).

Recent studies of malignant transformation by viral oncogenes and activated cellular oncogenes suggest that the transformation of cells to malignancy may require activation of more than one cellular oncogene. It is thus possible that the long "latent" period that characteristically elapses between radiation and the clinical appearance of a cancer may result from the need for successive oncogenes to be activated or for other types of sequential changes to take place.

C. Environmental and Life Style Risk Factors

It has been inferred that as much as 75-80% (3) of fatal cancers in the United States results from the influence of life style and other non-hereditary, or environmental, factors. Epidemiological studies imply that the largest effects are related to smoking, alcohol consumption, diet and other factors related to life style. Occupational exposures and the effects of radiation, chemical pollution, medical therapy, sexual activity, and infections are thought to contribute to a lesser extent. In some instances, heredity may render an individual more vulnerable to the effects of an

environmental carcinogen, as is illustrated by the heightened suscepti-
bility of individuals suffering from xeroderma pigmentosum to the develop-
ment of skin cancer as a result of exposure to the ultraviolet radiation
in sunlight. In evaluating the importance of the various environmental
risk factors, one should consider the potential influence of host-related
characteristics as well as the possibility that a cancer may have multiple
causes.

1. Smoking

Smoking of tobacco, particularly in the form of cigarettes, is
generally recognized as the single most important external risk factor
for human cancer, being estimated to cause 25-40% of all cancer deaths in
the U.S. (3,11,12). It is the primary cause of lung cancer in both men
and women, and is also associated with an increased risk of cancer of the
larynx, oral cavity, esophagus, bladder, kidney, and pancreas. Although
the percentage of the smokers in the population has declined from 42% in
1965 to a current level of approximately 33%, the number of active smokers
in the United States is estimated to be about 53 million (12), and there
is concern about the potential risks from "passive" smoking in non-smokers
(13-15). Although the specific mechanism(s) by which tobacco smoke
contributes to an increased risk of various types of cancer is not yet
known, a variety of carcinogenic chemicals are known to be components of
tobacco smoke (12).

2. Alcohol consumption

Alcohol consumption is thought to play a role in the onset of
cancer at a variety of sites, including the mouth, pharynx, larynx,
esophagus, liver, and lung; and some investigators have associated 3-5%
of all cancer deaths with the drinking of alcoholic beverages (3). Al-
though approximately one-third of the adult U.S. population drinks alcoho-
lic beverages at least once a week, and about 10 million members of the
population are estimated to be problem drinkers (4), the specific impact
of alcohol per se on human cancer risk is difficult to assess since,
among the complexities, reliable quantitative data on consumption are
difficult to obtain. Furthermore, many investigators believe that alcohol
acts chiefly by enhancing the effects of other primary carcinogens such
as those in tobacco smoke (4).

3. Diet

Although there is a growing recognition that diet can influence the
risks of specific types of cancer, the mechanisms and magnitudes of
dietary effects are poorly understood. Doll and Peto infer that diet may
be involved in 10-70% of all cancers in this country (3). Humans are
exposed to a multitude of agents that can enhance or inhibit the onset of
cancer, through the dietary intake of meats and fats, fibers, vitamins,
and naturally occurring carcinogens and their precursors (16). Carcinogens
in the diet also arise as by-products of food preparation (polycyclic
aromatic hydrocarbons), or may be introduced as natural contaminants

(aflatoxin), environmental contaminants (pesticide residues, heavy metals, PCBs, etc.), and additives for coloring, flavor (cyclamates and saccharin), and food preservation. Dietary carcinogens may act as tumor initiators or promoters, may facilitate the formation of carcinogens in the body, or may affect the transport, activation, or deactivation of carcinogens already present in the body (4).

4. Occupational exposures

Exposure to various occupational risk factors can increase the likelihood of cancer. Carcinogens that have been identified in the workplace include arsenic, asbestos, benzene, coal tar pitch volatiles, 2-naphthylamine, vinyl chloride, nickel and radiation. Moreover, there are a number of industries such as the petrochemical industry, the rubber industry, and coal mining, in which workers seem to have an excess risk of developing cancer, even though the specific risk factor or agent has yet to be identified. Because of the relatively long latencies associated with most forms of occupationally related cancers, current incidences of, or deaths from, occupationally related cancers are typically the result of exposures that occurred one or more decades in the past, when exposure levels were usually much less well-controlled and not as well-documented as are present-day levels. Furthermore, since workers frequently change jobs, both within and between industries, they may be exposed to a variety of potentially carcinogenic agents, the individual effects of which are not easily isolated.

5. Pollution

Manmade pollution of air and water is another source of potential cancer risk for humans. The frequently observed increase in lung cancer death rates among inhabitants of the more urban areas of the United States has been interpreted as evidence that air pollution, primarily polycyclic aromatic hydrocarbons from auto exhaust contributes to the risk of cancer. This argument is confounded, however, by the fact that the typical urban dweller is more likely to smoke than his rural counterpart and more likely to come into contact with a variety of occupational/ industrial risk factors as well. Although it is extremely hard to separate the impact of polluted air from the effects of these other risk factors, most researchers seem to believe that the actual percentage of all cancers specifically attributable to air pollution, while perhaps not negligible, is likely to be small (4).

The carcinogenic effects of water contamination, which may arise as a result of industrial pollution, agricultural runoff, waste dump seepage, and as a byproduct of drinking water purification (17), are even more difficult to assess than those associated with air pollution (4). Even in the few instances where case-control studies have been conducted, results have not always been consistent (4).

6. Medical therapy and diagnosis

Some agents used in the past to diagnose or treat various diseases have subsequently been shown to increase the risk of cancer, and their their use has been curtailed. Examples include inorganic trivalent arsenic (skin cancer), chloronaphazine (bladder cancer), the radioactive contrast agent, thorotrast (cancer at the organ of concentration), and diethylstilbestrol (vaginal adenocarcinoma) (4). Ionizing radiation and some of the drugs that have been found to possess carcinogenic potential, such as certain alkylating agents used to treat different types of cancer and various immunosuppressive drugs employed in organ transplantation, continue to be used with discretion, insofar as their expected benefits are considered to outweigh their known risks.

7. Sexual development and behavior

Hormonal stimulation associated with normal sexual development influences the risk of cancer in humans. For example, the risk of breast cancer in women is affected by age at menarche, age at first childbirth, and age at menopause. The incidence of testicular cancer is elevated in men born with cryptorchidism or undescended testes. The likelihood of developing cancer of the uterine cervix increases with the number of different sexual partners that a woman has had (4).

8. Viral infections

Viral infections are a known cause of various cancers in animal species and have been regarded as potential risk factors in the development of human tumors. The Epstein-Barr virus is thought to act as a causative cofactor in the onset of Burkitt's lymphoma (in Central Africa and New Guinea) and nasopharyngeal carcinoma (in the Far East, especially South China). Hepatitis B virus evidently plays a role in the development of hepatocellular carcinoma, particularly in Asia and Africa (3,4).

Other viruses of possible importance in human reproductive tract cancer development include herpes simplex virus (4) and cytomegalovirus (4). Human T-cell leukemia virus (18) has been isolated and sequenced and is clearly the etiologic agent in this type of leukemia. At the present time, the role of retroviruses or oncogenes in other cancers is unclear, but it could well be that activation or mutation of oncogenes are important factors in the genesis of many cancers.

9. Interactive effects

The preceding discussion of carcinogenic risk factors concerned primarily the effects of individual agents, whereas humans are ordinarily exposed to a variety of agents. The potential for interactions among the effects of different risk factors should also thus be considered. The interaction of two factors can be expressed in a variety of ways. For example, one may act as a vector that carries the other to a critical target site; the first may promote or enhance the carcinogenic activity of the second; the two may act independently; or they may produce a joint effect which markedly exceeds the sum of their separate effects.

Although epidemiology has not focused to any great extent on inter-
active effects between suspected or known carcinogenic risk factors,
there are a few well-known examples of such phenomena. It has already
been noted that alcohol consumption is generally regarded as a co-factor
that combines with cigarette smoking to elevate the risk of esophageal
cancer. Similarly, the joint action of infection with hepatitis B virus
and dietary intake of aflatoxin has been cited as a cause of liver cancer
in certain African and Far Eastern populations. Dietary zinc deficiency
may also interact with alcohol consumption to increase the likelihood of
developing esophageal cancer (4). Furthermore, some investigators have
suggested that air pollutants combine with carcinogens in cigarette smoke
to enhance the production of lung cancer (4). However, the most striking
example of an enhanced response resulting from the joint action of two
environmental carcinogens is the combined effect of asbestos and cigarettes.
The mortality ratios for workers exposed to either asbestos or cigarettes
individually were observed in one industrial study to be approximately 5-
and 10-fold, respectively, whereas the corresponding ratio for workers
exposed to both (i.e., asbestos-exposed workers who smoked) was in excess
of 50-fold (4). Cigarette smoking also appears capable of altering the
carcinogenic effects of ionizing radiation in certain circumstances, as
is discussed in a later section of this report (Chapter IV-H).

REFERENCES - Chapter II

1. Weinstein, I. B., Current Concepts and Controversies in Chemical Carcinogenesis. J. Supramol. Struct. Cell. Biochem. 17: 99-120 (1981).

2. Weinstein, I. B., Carcinogen Policy at EPA (letter to the Editor). Science 219: 794-796 (1983).

3. Doll, R. and Peto, R. The Causes of Cancer: Quantitative Estimates of Avoidable Risks of Cancer in the United States Today. J. Natl. Cancer Inst. 66: 1191-1308 (1981).

4. Office of Technology Assessment, "Assessment of Technologies for Determining Cancer Risks from the Environment." U.S. Government Printing Office, Washington, D.C., 1981.

5. Marx, J. L., What Do Oncogenes Do? Science 223: 673-676 (1981)

6. Bishop, J. M., Cancer Genes Come of Age. Cell 32: 1018-1020 (1983).

7. Sukumar, S., Notario, V., Martin-Zanca, D. and Barbacid, M., Induction of Mammary Carcinomas in Rats by Nitrosomethylurea Involves Malignant Activation of H-ras-1 by Single Point Mutations. Nature 305: 658 (1983).

8. Sukumar, S., Pulciani, S., et al., A Transforming ras Gene in Tumorigenic Guinea Pig Cell Lines Initiated by Diverse Chemical Carcinogens. Science 223: 1197-1199 (1984).

9. Rowley, J. D., Oncogen: Human Oncogene Locations and Chromosome Aberrations, News and Views. Nature 301: 290-291 (1983).

10. Guerrero, I., Villasante, A., Corces, V. and Pellicer, A., Activation of a c-K-ras Oncogene by Somatic Mutation in Mouse Lymphomas Induced by Gamma Radiation. Science 225: 1159-1162 (1984).

11. Jett, J. R., Cortese, D. A. and Fontana, R. S., Lung Cancer: Current Concepts and Prospects. Ca - A Cancer Journal for Clinicians 33: 74-86 (1983).

12. U.S. Department of Health and Human Services, "Cancer: The Health Consequences of Smoking: A Report of the Surgeon General." U.S. Government Printing Office, Washington, D.C., 1982.

13. Hirayama, T., Non-smoking Wives of Heavy Smokers have a Higher Risk of Lung Cancer: A Study in Japan. Br. Med. J. 282: 182-185 (1981).

14. Trichopolous, D., Kalandidi, A., Sparros, L. and MacMahon, B., Lung Cancer and Passive Smoking. Int. J. Cancer 27: 1-4 (1981).

15. Correa, P., Pickle, L. W., Fontham, E., Lin, Y. and Haenszel, W., Passive Smoking and Lung Cancer. Lancet 2: 595-597 (1983).

16. Ames, B. M., Dietary Carcinogens and Anticarcinogens. Science 221: 1256-1264 (1983).

17. Hogan, M. D., Chi, P., Hoel, D. G. and Mitchell, T. J., Association Between Chloroform Levels in Finished Drinking Water Supplies and Various Site-Specific Cancer Mortality Rates. _J. Exp. Pathol. Toxicol._ 2: 873-887 (1979).

18. Popovic, M., Sarin, P. S., Robert-Gurroff, M., Kalyanaraman, V. S., Mann, D., Minowada, J., and Gallo, R. C., Isolation and Transmission of Human Retrovirus (Human T-Cell Leukemia Virus). _Science_ 219: 856-859 (1983).

Chapter III: RADIATION AS A CAUSE OF CANCER

A. Introduction

Although ionizing radiation has been a part of the natural environment since the world began, only within the past century has man begun to study and use radiation as a tool in industry, biology, medicine, and warfare. The study of ionizing radiation as a cause of cancer has been particularly productive, with the result that we probably know more about its carcinogenic effects than about those of any other environmental carcinogen (1). This knowledge has been gained because it has been possible to identify study populations with documented exposures to fairly high radiation levels, and because ionizing radiation has proved to be a precisely controllable means of inducing cancer experimentally in laboratory animals. As a public health problem, ionizing radiation ranks well down the list of carcinogens: less than 3% of the U.S. cancer burden can be plausibly attributed to ionizing radiation from natural sources and human activities (2), compared to around 30% for tobacco smoking (3). We also know, however, that large doses of ionizing radiation can noticeably increase the cancer risk, and we are able to quantify these effects with some confidence (4). For example, among 6,035 atom bomb survivors in the Life Span Sample who were exposed to 100 or more rad, there were 498 deaths from cancer in the period 1950-1978, when only 323 such deaths would have been expected on the basis of the experience of survivors exposed to less than one rad, an increase of 54 per cent (5). Among the 23,073 exposed to 1-9 rad, however, the observed 1,248 cancer deaths are no higher (even slightly less) than expected on the same basis.

B. Characteristics of Ionizing Radiation

Ionizing radiation includes electromagnetic radiation (such as X rays and gamma rays), and energetic subatomic particles (such as protons, neutrons and alpha particles). These radiations have the capacity to produce ions from atoms or molecules in their paths by adding or removing electrons. A mechanism by which ionizing radiation induces cancer is thought to begin with the absorption of energy within cells, leading to alterations in the genome of the cell (1; see also Chapter II). Some other forms of radiant energy, like ultraviolet light, can affect cellular DNA directly and induce cancer, but not by ionization.

The energy absorbed per unit mass from the radiation traversing a tissue is termed the absorbed dose. Absorbed dose (or, for simplicity, dose) is measured in rad (1 rad = 100 erg per gram) or gray (1 gray (Gy) = 1 joule per kg = 100 rad). In general, the greater the dose, the greater the likelihood of an observable biological effect. Different biological effects can interfere with one another, however; e.g., it is possible for the likelihood of cancer to decrease with increasing dose at very high dose levels if cells that might otherwise give rise to cancer are so severely damaged that they lose the ability to multiply (1,4,6).

Different types of ionizing radiation have been compared experimentally with respect to various biological effects, including cell killing, mutagenesis, and carcinogenesis (6). In general, the relative biological effectiveness (RBE) of a given absorbed dose of charged particle radiation depends on the spatial density of the ionizations (linear energy transfer, or LET) produced along the tracks of the radiation, the heavy particle radiations tending to produce very closely spaced ionizations (high LET), while electrons, X rays and gamma rays tend to have fewer ionizations per unit length of track (low LET). In dealing with different types of radiation, the practice in radiation protection has been to relate the doses and effects of a given high-LET radiation to those of 250 kVp X rays as a standard, by introducing the quantity "dose equivalent." For a given end point, e.g., 50% acute mortality, the RBE of a certain type of radiation, say, neutron radiation of a given energy, is defined as the ratio of the required dose of X rays to the required dose of neutrons for that end point. For other end points, for different energies and for different dose rates or total doses, the RBE will have different values. A variable RBE is difficult to use for radiation protection purposes, and therefore practical reliance for assessing the impact of occupational or environmental exposures to high-LET radiation has been placed on a "quality factor", Q, which varies in relation to LET and is assumed to remain constant in the low-dose range (7,8). By multiplying the absorbed dose (in rad) by the quality factor (Q) for a given radiation, one obtains the "dose equivalent" for that type of radiation (expressed in rem = "rad equivalent in man"). The use of the Q factor is unsatisfactory, however, for the purpose of estimating cancer risk from high-LET radiation, in view of the aforementioned variations in RBE. In general, data are not available for estimating the site-specific RBE for each particular set of circumstances;[1] the necessary information includes the LET of the radiation at the target tissues. For internal emitters (deposited radionuclides), knowledge of the spatial and temporal distribution within the target tissue will also be required. These are factors that must be determined on a case-by-case basis. For this reason, the Working Group has refrained from making tables for high-LET radiation except in the limited case of alpha particle radiation from radium-224 in bone and exposure to radon daughters in the case of lung, for which epidemiological data exist from direct observations.

C. Sources of Radiation Exposure

Each of us is continually exposed to ionizing radiation from cosmic rays, disintegrating radioactive elements in the earth, and radioactive elements occurring naturally in our bodies (4). People living at sea level in the United States receive about 80 millirem (1,000 millirem = 1 rem) average dose (strictly speaking, average dose equivalent) to their internal organs per year (Fig. III-1); but at higher elevations, where cosmic rays are more intense, or in regions where the natural radioactivity of the soil is fairly high, the dose can be twice that size, or greater. Natural background radiation is increased by building materials

---

[1]The NCRP and ICRP-ICRU currently have task groups working on high-LET radiation.

containing radioactive minerals. People in poorly ventilated buildings are exposed to elevated levels of the radioactive gas radon, given off by building material and by the natural radioactivity in the underlying soil (9,10). The average dose equivalent to the bronchial epithelium, which reflects exposure to radon, is now thought to be 3 rem annually (11). This represents an increase of the previous estimate of 0.5 rem and reflects (a) a decision to employ a quality factor of 20 in place of the factor of 10 previously used, and (b) recent measurements of the indoor exposure to radon daughters inhalation, which has increased because of reduced exchange with the outside air.

Average radiation doses from man-made sources are of the same order of magnitude as from natural background, about 100 millirem per year (4). By far the largest contribution is from medical diagnosis. Individuals receiving radiation therapy for benign or malignant disease can get very large doses to certain parts of the body, up to several thousand rad, but relatively few people get such treatment. Similarly, the number of people occupationally exposed to ionizing radiation is not large and, because the average exposures are within a few hundred millirem per year, the contribution to the population average is quite small (4). The dose from global fallout produced by nuclear weapon tests and from radiation-emitting components of consumer products like television sets and smoke detectors is negligibly small (4,6,12).

D. The Evidence for Radiation Carcinogenesis in Man

We know that ionizing radiation can cause cancer in man because studies of different populations with documented exposures to high radiation levels (hundreds or thousands of times natural background) have consistently found higher cancer rates than those seen in comparable, non-exposed populations (13). Ionizing radiation was used in diagnosis and to cure or alleviate the symptoms of disease long before its carcinogenic potential was fully appreciated, and is the treatment of choice for some diseases (including cancer) for which the potential benefit outweighs the risk of subsequent cancer.

Studies of patient populations highly exposed to X radiation during diagnostic or therapeutic procedures constitute much of the epidemiologic basis for our knowledge of radiation carcinogenesis (14). Information on the effects of alpha-particle radiation comes from studies of workers who ingested radium while painting instrument dials with luminous paint (15) and from studies of uranium and other hard-rock miners working in atmospheres heavily contaminated with radon (16-17). There have been intensive studies of the survivors of the atomic bombings of Hiroshima and Nagasaki in 1945 (5), and of natives of the Marshall Islands, who in 1954 were exposed to radioactive fallout from a nuclear weapons test in the Pacific (18). The largest number of persons studied who were exposed to low-LET radiation at low dose and dose rate were patients who received oral iodine-131 for the treatment of hyperthyroidism (19).

From many studies it appears that, at some level of exposure, ionizing radiation can increase the risk for many, and perhaps most, of the types of cancer that occur in man. In general, it is clear that

radiation does not create unique forms of cancer, but increases the risk
of some cancers that occur naturally. For the acute forms of leukemia,
chronic granulocytic leukemia, and female breast cancer, the association
is so strong as to appear certain (4). There is fairly strong evidence
that ionizing radiation does not cause chronic lymphatic leukemia (4,6).
For most other forms of cancer, the evidence lies somewhere between these
two extremes, although for many the position on this scale is uncertain
because there is very little information.

The credibility of a presumed causal association between risk and
radiation exposure depends upon several factors, which must be considered
in evaluating the evidence that radiation exposure affects risk for a
particular cancer site:

1) Statistical significance – This depends on the total
number of cancer cases observed and the apparent size of
the excess relative to the baseline risk. For a fixed
number of cases, the strength of the association is
greater if the excess risk is relatively large and, for
a fixed relative excess, the association is more credible
if the evidence is based on many cases.

2) Specificity – How certain is it that the association
was not due to something else? Credibility is helped by
comparison with a non-exposed population, otherwise similar
to the exposed population. It is especially important to
satisfy this requirement in studies of medically exposed
populations, for which the conditions leading to exposure
may themselves be related to the risk of subsequent cancer.
Since population groups that have been exposed to radiation
actually differ in many ways from the general population,
differences in rates of disease from general population
rates may be difficult to interpret or to attribute to the
radiation exposure.

3) Dose response – The level of risk should appear to
increase with increasing radiation dose to the tissue
of interest. Each of us is exposed to natural background
radiation at the very least, and so the concept of increased
risk from additional exposure involves the assumption of a
gradient of risk with increasing exposure. As already
mentioned, it is always possible that an increased risk among
medically exposed persons may be attributable to the reasons
for exposure rather than to the exposure itself. This possibility
is less likely if there is an association of risk with level of
exposure among the exposed persons.

4) Consistency – Is the association seen in a number of
exposed populations, and are the apparent excesses similar
when such factors as dose, age, and period of observation
have been taken into account? "Statistically significant"
associations will occur as a consequence of mere chance in a
small proportion of studies – and in the field of radiation
carcinogenesis the number of studies is large. Further, spur-

ious associations can arise by chance between cancer risk and practically anything, or exposure can be fortuitously related to a true risk factor. But such spurious associations are very unlikely to arise in many different populations, exposed under different circumstances. .We therefore tend to place most credence in associations that turn up frequently and under diverse circumstances of exposure, while distrusting isolated reports not verified by other experience.

E. Quantification of Risk

Partly because we cannot tell for certain whether or not a person will develop cancer, even when we have the most detailed information possible about that person's physical condition, genetic background and life experiences, and partly because, in our present state of knowledge, carcinogenesis seems to be largely a random process, it is useful to think in terms of probabilities. In other words, whether or not a person develops cancer, and the time when that cancer becomes detectable, are matters of chance. Most of what we know about cause-effect relationships and cancer rates in different population subgroups is useful to the extent that it tells us how the probability of cancer diagnosis in a given person at a given time depends upon certain observable facts. Thus, information that ionizing radiation is associated with a particular type of cancer should, if it is to be of any help to us, lead to improved estimates of the probability that cancer will occur following radiation exposure.

It is not possible to tell whether or not a particular cancer observed in a given individual following exposure to ionizing radiation was caused by that exposure. Cancers occur in nonexposed people and are in general indistinguishable from radiation-induced cancers. We often can tell, however, if the number of cancers observed in a group of exposed people is greater than the number that would have been observed in the absence of exposure and, if so, we can estimate roughly how many of the observed cancers were induced by radiation. Thus we can estimate the excess risk, in an average sense, that pertains to any similar group of exposed people. Such an estimate pertains to a single individual only to the extent that that person can be considered "typical" of the group from which the estimate was obtained. In a particular case of radiation exposure, one must consider a number of relevant factors, including radiation dose; sex; age at exposure; time following exposure; and additional risk factors or modifiers.

F. Sex

For some organ sites, baseline cancer rates vary markedly by sex, while for others there is no real difference. Sensitivity to the carcinogenic effects of ionizing radiation also varies by sex and not always according to the pattern of natural rates. Sex differences in sensitivity seem to mirror differences in natural rates for leukemia and for thyroid and breast cancer. For cancers that vary between sexes because of differing exposures to carcinogens other than ionizing radiation (e.g., cigarette smoking in the case of lung cancer) sex differences in sensitivity to radiation otherwise may be small or nonexistent (4). Although many

populations studied for radiogenic cancer risk are wholly or predominantly
male or female, the roughly equal sex distribution of the Japanese A-bomb
survivor population allows sex-specific risk estimation for most cancer
sites for which a radiation related risk has been established (4).

G. Age at Exposure

        One of the most interesting observations to come out of the Japanese
A-bomb survivor studies, which are based on a large population of all ages
in 1945, is that the risk of radiation-induced cancer depends strongly on
age at exposure (5,20). This dependence is complicated by a strong re-
lationship between age and the time from exposure to cancer diagnosis but,
in general, children appear to be more sensitive to radiation than are
adults. This pattern has long been recognized for leukemia, for which we
appear to have a more or less complete picture of the excess risk among
A-bomb survivors (21,22). All age groups experienced a temporary increase
in leukemia risk, which was higher relative to the baseline risk among the
very young. In terms of the absolute number of leukemias per capita,
however, the excess among the oldest group was fully as high as that in
the youngest group (Fig. III-2).

        The pattern of age dependence has emerged only gradually for the
solid tumors, as A-bomb survivors exposed as children have reached ages
at which cancer is ordinarily an important contributor to mortality.
Relative to baseline cancer rates, radiogenic cancer risk appears to
decline with increasing age at exposure. This pattern is very clear for
cancer of the female breast (Fig. III-3) and for the thyroid, but it also
seems to hold for all solid cancers as a group (Fig. III-4). There is
clear evidence of an excess risk following exposure after age 50 for
leukemia and for digestive and other cancers (5), but not for cancers of
the female breast and thyroid (23,24). In general, observations on other
exposed populations are consistent with those obtained from the A-bomb
survivors, but do not have a similar breadth of coverage with respect to
age (4).

        The bulk of epidemiological data on cancer risk in populations
exposed to ionizing radiation is based on follow-up of 35 years or less.
For many cancer sites, no excess risk is discernible until ages at which
baseline population rates are appreciable, and as a result, risk esti-
mation for persons exposed at very young ages can be difficult because,
so far, observations are few. For example, it was not until very recently,
when follow-up of the Japanese A-bomb survivors and thymically-irradiated
children in the United States was extended to 35 years or so, that it
became clear that there was an excess risk of breast cancer associated
with radiation exposure in early childhood (25,26). Age-specific risk
estimates for cancers of the esophagus, intestine, and pancreas were
formulated by the BEIR III Committee through the expedient of assuming
that radiogenic digestive cancers as a group share a common pattern of
variation by age at exposure (4). Without such an assumption, it is
difficult to justify estimates for these cancer sites following exposures
at young ages. Reasonable estimates can be calculated, however, for
leukemia and cancers of the thyroid, breast, bone and salivary glands.

Although an association appears to be well established between prenatal X irradiation and childhood cancer, the extent to which the association may be causal is highly controversial (4,27-29). More precisely, it is difficult to reconcile an order-of-magnitude difference between risk estimates derived from studies of the frequency of X-ray pelvimetry, usually carried out shortly before birth (4, page 452) and estimates derived from studies of patients given therapeutic X-radiation during infancy (30), or A-bomb survivors exposed in utero (31) or in early childhood (5). It is not readily apparent that the association is explainable in terms of a medical indication for pelvimetry that itself confers an increased risk of childhood cancer; analyses adjusting for variables such as birth weight, maternal age, and a few others, have not greatly affected risk estimates (29,32). Furthermore, analyses restricted to twin births, for which medical indication for pelvimetry should be less important, have yielded estimates similar to those not restricted to twins (33,34).

Experimental studies do not support a greater cancer risk from prenatal as opposed to postnatal exposure to ionizing radiation (4,35,36). A particularly thorough experimental investigation of the influence of age at exposure on cancer risk has been carried out by Sasaki et al. at the National Institute of Radiological Sciences in Japan (37-40). These studies indicate that mice irradiated with X or gamma rays at fetal, perinatal, neonatal, pubertal, and young adult stages of development vary with respect to the type and frequency of tumors developing after irradiation. The observed differences suggest, however, a smooth variation by exposure age and, in particular, little if any difference between exposure at the late fetal, neonatal, and suckling stages. Irradiation during the middle intrauterine stage, on the other hand, was followed by significantly lower cancer risk than that observed among non-irradiated controls, especially for tumors of lymphoreticular tissue, the lung, and, in females, the uterus (38).

H. Time to Response

The plausibility of a causal association between a cancer and a prior exposure of the patient to ionizing radiation depends partly upon the length of time by which diagnosis follows exposure. Detection is unlikely until hundreds of millions of cancer cells have been replicated from what probably begins as a single transformed cell. Moreover, for many, but not all, types of cancer the epidemiological evidence suggests that events subsequent to irradiation may be required before any cellular changes initiated by ionization can result in a transformed cell capable of uncontrolled proliferation. Thus, for example, in irradiated populations no excess risk of breast cancer or lung cancer has been seen until the exposed individuals have reached ages at which these cancers usually are observed in non-irradiated populations, which suggests that cancers of these sites require other time-dependent etiologic factors whether or not exposure to ionizing radiation plays a role in their causation. Bone cancer and leukemia, on the other hand, have appeared in excess within a very few years after exposure in heavily irradiated populations, suggesting that subsequent events follow rapidly, or may not be required to complete

the carcinogenic process. Another marked contrast that distinguishes
leukemia and bone cancer from most other cancers that have been identified
as radiation-related is that leukemia and bone cancer risk appears to
return to near-normal levels within a period of 30 years or less after
irradiation, whereas for other types of cancer, the period of increased
risk is much longer and may extend to the end of life.

Reports of expert committees concerned with cancer risk from ionizing
radiation have dealt with response time mainly in relation to lifetime
estimates of risk, a purpose for which sophisticated modelling is not
always necessary. For example, in the 1980 BEIR report, radiation-induced
leukemia and bone cancer were judged to have limited expression periods
following an exposure of brief duration and lifetime risk was calculated
as if excess risk were constant during the third to 29th years after expo-
sure and zero before and after (4). This "plateau" model gave about the
same lifetime risk as would have been obtained from a biologically more
reasonable model. We know, however, as did the BEIR Committee, that
leukemia and bone cancer risk increase over time to a peak followed by a
more gradual decline, and that (for example) a radiation-induced bone
cancer is much more likely to be diagnosed during the 10th year after
exposure than during (say) the 4th or 28th years. The plateau model is
thus unsuitable for calculating probability of causation, and should be
replaced by models that more closely reflect observed temporal patterns.

The BEIR Committee rejected a plateau model of finite length for
cancers other than leukemia and bone cancer, because after approximately
30 years of follow-up in the major exposed populations, excess risk has
shown no sign of declining. It was noted that evidence of an excess risk
was much slower to develop than for leukemia and bone cancer, however,
and the first 10 years after exposure were ignored in the risk calculations.
Alternative models were used to project estimated risk beyond the period
of follow-up to the end of life. The "absolute risk" model is a plateau
model that extends to the end of life; in other words, given that an
exposure of brief duration has caused a cancer, the time to diagnosis in
different members of the population is assumed to be uniformly distributed
over the remainder of life following the minimum response time, assumed
by the BEIR Committee to be 10 years. This projection model was used in
parallel with the "relative risk" model, so called because the ratio
between the risk of a radiation-induced cancer and the average risk in
the absence of exposure, as determined from population rates, is assumed
to be the same for each year of life following the minimal response time.
Under the relative risk model, therefore, the distribution of response
time is non-uniform, varying in proportion to baseline rates which depend
upon age at observation.

Depending upon age at exposure, lifetime risk projections according
to the absolute and relative risk models can vary markedly, with the
greatest deviation corresponding to young exposure ages. Averaged over
all exposure ages, the relative risk model lifetime projection on the
basis of follow-up data now available tends to be about 3 times as high
as the absolute risk model lifetime projection (4), because population
rates for the most important cancers tend to increase steeply with increas-
ing age. Even during the first 30 years or so after exposure, for which
the total excess risk estimated by the two models must agree because this

is the length of the follow-up period on which the risk estimates were
based, the models differ with respect to the likelihood that a radiation-
induced cancer will occur in any given year. For example, the 1980 BEIR
report estimated that, for a 100-rad exposure at age 15, the average ex-
cess breast cancer risk during years 11-30 following exposure (i.e., from
age 25 through age 44) is 730 cancers per year per million women exposed
(4, page 198). Ignoring intercurrent mortality, about 14,600 extra
breast cancers would be predicted during this period under either pro-
jection model, compared to about 10,000 which would be expected according
to population rates. But the distribution of the excess cases differs
markedly by model. The U.S. incidence of breast cancer per million women
(i.e., the number expected to develop breast cancer at a given age) is
about 64 at age 26, 435 at age 35, and 1,314 at age 44 (41). The absolute
risk model would predict 730 excess cancers at each of these ages following
a 100-rad exposure at age 15, while the relative risk model would predict
93 at age 26, 635 at age 35, and 1918 at age 44. Looked at in another way,
in a population exposed to 100 rad to breast tissue, 92% of the total
breast cancer risk at age 26, or 730 out of 794 cases predicted according
to the absolute risk model, would be radiation-related compared to 63% of
those at age 35 and 36% of those at age 44, while according to the relative
risk model, 59% of all breast cancers observed at each of these ages would
be considered radiation-related.

Probability of causation calculations, which pertain to a particular
cancer diagnosed at a particular time following a particular radiation ex-
posure, clearly require an approach to response time that is more refined,
and less ambiguous, than that of the BEIR Committee. A number of authors
(42-44) have suggested that the lognormal model applied by Sartwell (45)
to the incubation period for infectious disease may be appropriate for
radiation-induced cancer. This suggestion seems reasonable for those
cancers, like bone cancer (46) and leukemia (47), that have been observed
to follow a wave-like pattern of an increase in risk followed by a decline;
it seems less plausible, or less practicable, for cancers of sites like the
lung, female breast, and digestive tract, for which radiation-related ex-
cess risks were slow to become apparent and showed no signs of declining at
last follow-up (5).

Epidemiological data permit response-time analyses for only a few
cancer sites; the crucial considerations are (a) a high excess relative
to background, i.e., so high that most of the cancers diagnosed following
exposure can be assumed to be radiation-related; (b) an exposure of brief
duration; and (c) a lengthy follow-up period. These criteria are satisfied
best for bone cancer data from a German population given therapeutic in-
jections of radium-224, a bone seeker with a half-life of 3.6 days.
Fifty-three bone sarcomas were observed compared with only 0.2 expected,
so that essentially all the cases can be considered to be radiation-induced,
and treatments lasted less than one year (46). Less pure, but nevertheless
useful, data pertain to leukemia (21) and breast cancer (48,49) among A-bomb
survivors. The criteria are satisfied to a lesser extent by lung cancer
mortality among A-bomb survivors (5,49) and breast cancer incidence in
patients treated by X rays for acute postpartum mastitis and in tubercu-
losis patients given multiple chest fluoroscopies (50), and marginally by
stomach cancer among A-bomb survivors (5,51). Thyroid cancer presents
special difficulties because it is usually an indolent disease which may

go undetected for a long time unless special efforts have been made at detection, as has been the case for A-bomb survivors and practically every other irradiated group in which an excess has been demonstrated. Thus the somewhat anomalous finding of a continuing observation of an excess among A-bomb survivors who were under 20 years old in 1945, and an apparent disappearance of excess risk over time among older survivors (24), could conceivably be an artifact of screening in which cancers that might otherwise have been discovered in recent years had been picked up earlier through improved surveillance.

Schematic representations of leukemia risk as a function of time after exposure based on A-bomb survivor data resemble lognormal or gamma distributions. These distributions, moreover, may differ by histological type and age at exposure (47). Formal statistical comparisons of dates of diagnosis among heavily exposed A-bomb survivors with those among lightly exposed survivors or non-exposed residents of Hiroshima and Nagasaki are consistent with this interpretation (48).

Comparisons of response time distributions between cancers of the breast, lung and stomach among heavily exposed persons and otherwise similar persons with little or no exposure are remarkable for the similarity they reveal (5,49,51). That is, heavily exposed persons have more cancers of the breast, lung, and stomach than they would otherwise have, but the temporal distributions of the excess cancers are not distinguishable from those of non-radiogenic cancers. This finding is plausible in terms of a multi-stage model for carcinogenesis, in which radiation produces an early-stage change that can also be produced by other common agents, and in which late-stage changes are caused by events that are highly age-dependent. If, in fact, the likelihood of early-stage changes for these sites declines with increasing age in about the same way that the relative risk of radiation-induced cancer declines with increasing age at exposure, and if the likelihood of late-stage changes increases with increasing age in about the same way as population cancer rates increase with age, the observed temporal patterns of radiation-induced and baseline cancer rates following a radiation exposure should be very similar (52).

Congruence between radiation-induced and baseline cancer rates of the same site, in persons of similar ages at observation, with respect to temporal distribution of risk, is equivalent to the relative risk projection model used by the BEIR III Committee. The relative risk projection model asserts that, for a cohort of persons of given age, after the passage of a necessary latent period, the relative risk of radiation-induced cancer is essentially constant. It is inconsistent with the absolute risk model, according to which the relative frequency of radiation-induced cancers compared to baseline cancers should decline over time for those sites for which baseline cancer rates increase with age, and it is also inconsistent with another model, proposed by Gofman (53), in which this relative frequency is assumed to increase for about 40 years after exposure, and then decline. The justification given by Gofman for this model is unconvincing: the increase with time in relative risk that he noted depended upon an analysis that ignored age; the increase was a consequence of cohort effects, in which increasing numbers of younger (and more radiation-sensitive) women entered upon the ages at which breast cancers occur. The decrease in relative risk postulated by Gofman is entirely speculative.

The hypothesis is inconsistent with available data within 35 years after exposure, and beyond that point there are no data with which to test it. When age-specific analyses are done on the data used by Gofman to support his model, no increase in relative risk with increasing follow-up is found (5,49,50).

Finally, minimal response time is an essential element of temporal distribution of risk, and one that is extremely difficult to estimate. If cancers are of monoclonal origin, as seems likely, the development of a radiation-induced cancer can be considered sequentially in terms of the transformation of an affected cell which then becomes capable of unrestrained proliferation, followed by a growth period involving 30 or so generations of replication resulting in hundreds of millions of cancer cells, at which point detection becomes likely (54). Observed doubling times for radiographically-monitored primary and metastatic tumors of various sites in human patients appear to be lognormally distributed, with considerable variation by type (metastatic vs. primary) and site (54). These observations, especially those of primary tumors, necessarily occurred after many generations of replication had already taken place, and it does not necessarily follow that the time required for the entire growth phase can be determined by extrapolation. Doubling time may well depend upon attained tumor size, the degree of vascularization, or upon variable factors not influenced by the existence of a tumor. Also, lognormality of the doubling time at any stage of tumor growth does not necessarily imply lognormality for the total time necessary for growth; for example, if the process were characterized by some degree of statistical independence between growth rates at different times, a more nearly symmetric temporal distribution would result.

Tumor doubling-time data are intriguing in their implications for radiation carcinogenesis as a multi-stage process. If tumor growth tended to begin quite soon after irradiation, a wave-like temporal pattern of excess risk might be expected on the basis of growth kinetics alone. If, on the other hand, the beginnings of tumor growth were distributed over time in such a way as to produce a constant ratio between excess and background risk, there should be an initial period of several years during which, due to growth kinetics, the relative excess slowly increases from an initial value of zero to its eventual value.

I. Models for Dose Response and Dose Rate

To predict the risk of cancer at a given radiation dose from empirical observations of effects at other doses, one must use a mathematical model relating cancer incidence to dose. Various mathematical models have been proposed for the purpose (4,6,55); however, the empirical data are so imprecise in most instances as to be compatible with any of the available theoretical models. Hence, the choice of the most appropriate model is a matter of expert judgement.

For carcinogenesis, in general, and radiation carcinogenesis in particular, there are strong grounds for questioning the assumption that the dose-response relationship has a threshold (4,6,56-59). The evidence that many, if not most, cancers arise from a single cell (60), the putative

role of DNA or chromosomal damage in carcinogenesis (61-66), the heritable nature of the neoplastic transformation in somatic cell lines, and the linear-nonthreshold nature of the dose-effect relationship for radiation-mutagenesis and chromosome aberration induction in the low-dose region (6,67) imply that radiation-induced damage to the DNA or to the chromosomes of a single somatic cell may, under certain conditions, exert a potentially carcinogenic stimulus, even at the lowest radiation exposure level.

The extent to which host factors such as immune surveillance can introduce a practical threshold by delaying the onset of detectable cancer beyond the life span cannot be calculated at present. The existence of a complicated series of enzymes that repair DNA does not favor any particular model for interpolation of cancer incidence at low doses of radiation, since repair does not operate with total effectiveness. In addition, unless other carcinogenic agents act through unrelated mechanisms, the heterogeneity of the human population and the baseline incidence of cancer are high enough so that any dose of radiation may be conceived to increase the risk of cancer in the most sensitive members of the population (68-70). For these and other reasons, the assumption of a threshold for radiation carcinogenesis is currently not considered to be tenable for purposes of risk assessment.

If we are interested in the risk from lower-dose exposures, it is necessary to have an extrapolation rule or dose-response model by which the estimated high-dose risk determines lower-dose risk estimates. A fairly simple rule is to assume that excess risk is proportional to the number of ionizations produced in the tissue at risk, that is, proportional to absorbed dose. This rule is equivalent to drawing a straight line from a point representing zero excess risk at zero dose (natural background radiation levels) to the point representing the excess risk estimated at whatever dose was received by the population studied (the so-called linear model). Other rules, not based on a simple proportionality between dose and risk, correspond to curved lines. A general model widely accepted in experimental and theoretical radiobiology for stochastic effects (mutagenesis and carcinogenesis) of low-LET radiation allows for an unspecified degree of positive curvature corresponding to interactions between two radiation tracks, and negative curvature, influential mainly at high dose levels, corresponding to the competing effect of cell inactivation (4). The model assumes that two ionizing events are more likely to produce a biological effect if they occur very close together than if they are separated; because ionizing events tend to be widely spaced along low-LET tracks, closely-spaced events are likely to be at the intersections of different tracks and their probabilities are approximately proportional to the square of dose. A frequently observed, and related, phenomenon is that acute exposures to low-LET radiation tend to be more effective than the same amount of radiation delivered continuously over time or delivered in several fractions separated by periods of time. This, too, is thought to reflect variations in the likelihood that two ionizing events will occur close together in time and space. Such an occurrence is less likely if the events are not simultaneous, because the damage caused by the first ionizing event may be repaired before it can interact with the damage from the second event.

The above considerations do not apply to high-LET radiation, for which close spacing of the ionizing events along the radiation tracks is the rule, rather than the exception. Both theoretical and experimental studies suggest that, for high-LET radiation, the dose-response tends to be linear but is modified by negative curvature, mainly at high dose levels, due to cell inactivation. The data also indicate that fractionated or protracted exposures to high-LET radiation tend to be no less effective than acute exposures for the induction of stochastic effects (4).

Data on laboratory animals can provide principles to guide extra-polation from effects at high radiation doses to predict effects at low doses. For measuring small effects, however, such large numbers of animals are required that no experiment has been performed on a scale that suffices to define the dose-incidence relationship for carcinogenesis in different organs at doses below 10 rad. Furthermore, in most species of laboratory animals that are convenient to use (mice, rats), the "natural" incidence of cancers differs markedly among strains, as do the shapes and slopes of the dose-incidence curves for radiation-induced cancers (6). In some strains of mice, for example, breast cancers occur spontaneously in nearly 100% of females, whereas the incidence is 1% or less in the females of other strains; the effects of radiation on the incidence of such cancers vary similarly. These differences among strains appear to depend on genetic variations which are magnified by the highly inbred character of laboratory mice. Because of the highly outbred character of the human population--in which the incidence of cancer appears to be influenced more by differences in the environment, diet, and lifestyle than by genetic factors--animal-to-human extrapolations are fraught with uncertainty. For this reason, quantitative risk estimates for man have generally relied primarily on human epidemiological data (4,6).

Epidemiological data are not very informative about the choice of a dose-response model, for the same reasons that low-dose data tend not to be informative about excess risk (71). This is true even when the possibility of high-dose cell inactivation is ignored. The two cancer sites for which linearity with low-LET radiation is strongly suggested, the thyroid and the female breast, are in fact the only two for which there is much direct evidence for an excess risk from external exposures under 50 rad (24,72,73). For other cancers, including leukemia, dose-response analyses using general models, in which details of curvature are not fixed in advance, tend to yield risk estimates with very wide confidence limits. Also, less general models with specified curvature, which may be located anywhere in the range from linear to pure quadratic, tend to fit the available data more or less equally but produce a great variation in the estimated risk at low dose levels (4,71).

The related phenomena of variable increases in risk per rad depending on dose or dose rate can be handled crudely by the use of a dose-rate reduction factor, according to which the effectiveness of a high radiation dose delivered at a low dose rate or in many fractions is assumed to be several times smaller than that of the same dose delivered acutely. A more refined method uses a linear-quadratic dose-response model in which the quadratic coefficient is assumed to depend on dose rate - that is, the model as given corresponds to acute exposures and the quadratic coefficient is reduced for protracted exposures. Various official bodies

have used different approaches. The United Nations Scientific Committee on the Effects of Atomic Radiation (6) used a dose-rate reduction factor of 2.5, while the National Council on Radiation Protection and Measurements (55) gave a range of 2-10 for this factor and recommended the use of a linear-quadratic dose-response function. The 1980 BEIR Committee chose a linear-quadratic model for low-LET radiation in which the excess risk is proportional to $D + 0.0086D^2$, where D is the dose in rad (4). The linear term (proportional to dose) dominates below a so-called crossover dose of 116 (= 1/0.0086) rad and the quadratic term (proportional to dose-squared) dominates above that dose. This crossover dose, which was obtained by curve-fitting to A-bomb survivor leukemia data, is consistent with those obtained for chromosome aberrations in circulating human lymphocytes and in a number of studies involving chromosome aberrations and mutations in experimental animals or mammalian cells in culture (74).

It is generally agreed (4,55) that the linear term of the linear-quadratic dose-response model is unaffected by dose fractionation and by variations in dose rate, and that the quadratic term should become smaller as fractionation increases or the dose rate decreases. Thus, the BEIR committee used only the linear term of the linear-quadratic model to estimate risk from continuous exposures to 1 rad per year (4). Based on the data for mutation production in Tradescantia by gamma radiation (55), it appears that one may reasonably apply the linear term alone to continuous exposures to low LET radiation at dose rates several orders of magnitude higher (e.g., 0.01 rad per hour which corresponds to about 90 rad per year continuous exposure).

For cancers of the breast and thyroid gland, linearity of the dose-incidence relationship is suggested by the available data. For example, the risk coefficients derived from the carcinogenic effects of high thyroid doses in infants treated for thymic enlargement (30) are similar to those derived from average thyroid doses of 9 rad in Israeli children treated with X rays for tinea capitis (73). Similarly, risk coefficients for breast cancer in A-bomb survivors are essentially the same whether derived from the effects of doses below 30 rad or from the entire range of doses (72); furthermore, the incidence of breast cancer per unit dose in women who received their irradiation in daily occupational exposures as dial painters (75) or in many small, widely spaced exposures during multiple fluoroscopic examinations of the chest appears to be essentially the same as in women who received their irradiation in a single instantaneous exposure to atomic bomb radiation or in a few brief exposures during radiation therapy (50).

The BEIR III Committee did not incorporate the competing effect of cell inactivation, mainly at high dose levels, into its risk calculations, although it did consider the problem theoretically (4, p. 182). There appear to have been three reasons for this: First, the Committee had great difficulty obtaining useful information by fitting even a linear-quadratic dose-response model to the available data, and better results could not be expected from a more complex model. Second, the Committee relied heavily on data from the studies of Japanese A-bomb survivors, for whom exposures were fairly uniform over the entire body. Doses high enough to reduce the carcinogenic response appreciably through the competing effect of cell inactivation might well be in the lethal range for

man when delivered to the whole body. Moreover, the A-bomb survivor data gave no clear evidence of a high-dose downturn in the carcinogenic response. Finally, the BEIR Committee was concerned mainly with applications to low-dose exposures, for which the competing effect of cell inactivation is not a serious consideration. Nevertheless, cell inactivation at high dose levels is a likely explanation for increases in leukemia risk that have been lower than would be predicted among patient populations given partial-body exposures, and partial-organ exposures in terms of active bone marrow, at therapeutic dose levels for the treatment of ankylosing spondylitis (76) and cervical cancer (77).

J. Modifying Effects of Other Exposures

The literature of experimental carcinogenesis abounds with examples in which a co-carcinogen or promoting agent has been found to modify the level of effect, or even the shape of the dose-response curve, for radiation carcinogenesis. Examples in the epidemiological literature are rare, but not unknown. Increased skin cancer risk was found among persons given epilating doses of X rays as children for treatment of tinea capitis, but the cancers occurred more commonly in those irradiated areas with high levels of exposure to sunlight, did not occur in blacks, and among whites occurred preferentially in persons with light complexions (78). Smoking and radon exposure were found to interact multiplicatively among U.S. uranium miners in the causation of lung cancer (79); that is, increased risk per unit radiation dose was many times higher among smokers than among nonsmokers. On the other hand, an additive rather than multiplicative interaction was found among Swedish iron miners (80) and Japanese A-bomb survivors (81). The similar excess breast cancer risks among Japanese A-bomb survivors and medically irradiated U.S. women (50) suggest that whatever causes American women to have about 5 times the lifetime breast cancer risk of Japanese women does not interact synergistically with ionizing radiation.

In summary, little is known about the influence of other physical and chemical agents on radiation-induced cancer risk in man, and what little is known is generally consistent with additive interactions, at least for low-LET radiation. The experimental literature suggests that synergistic relationships exist, but they are yet to be discovered in humans, and we do not know how important they are relative to other determinants of risk.

K. Extrapolation from One Population to Another

As mentioned above, epidemiological data relating cancer risk to radiation exposure come from a variety of exposed populations but predominantly from patients given diagnostic or therapeutic X radiation and the Japanese A-bomb survivors whose exposures were chiefly to hard gamma radiation. Basing risk estimates on these data requires assumptions about the comparability of the irradiated populations on which the estimates were based with the population to which the estimates are to be applied.

For example, the population rates not influenced by radiation exposure among the Japanese A-bomb survivors and their non-exposed, local comparison group are similar to the USA population rates for leukemia but far lower for breast cancer and far higher for stomach cancer (82). The question arises: Should the absolute excess risk attributable to radiation exposure, that is, the difference between total risk and that expected according to population rates, be assumed to be the same for an irradiated USA population as for a similarly exposed group of Japanese A-bomb survivors, or should the excess be scaled proportionally to the underlying population rates? Both these extrapolation rules are very simple, even crude, and there is little information to support more complicated rules.

In general, absolute excess leukemia risk appears comparable between Japanese A-bomb survivors and medically irradiated Western populations with similar doses at similar ages (4). Comparisons between the A-bomb survivors and two medically irradiated USA populations with respect to breast cancer risk suggest that the absolute excess risk is about the same in all three populations, for similar ages at exposure, in spite of a five-fold difference in the underlying population rates (50). At high dose levels, the excess stomach cancer risk among British patients given X ray therapy for ankylosing spondylitis was not much different from that in A-bomb survivors of similar ages at exposure (5,83,84).

Radiation is believed to affect an early stage of the multi-stage process that results in cancer at least for breast cancer and perhaps for other cancers as well. If that is so, then the effect of other agents which act at an early stage would be simply to <u>add</u> to the effect which results from radiation. That the causes of excess stomach cancer in Japan act on early stages is implied by the fact that among Japanese migrants to the United States, although stomach cancer rates do decline from the Japanese levels to those which characterize the host country, they do so only after a very long delay—several decades (85). The implication is that the initial events had already occurred before the migrant left Japan.

A possible contradiction between the constant relative risk model for time to response and the absolute risk model for projection from one population to another has been pointed out by Land et al. (50) and by the National Academy of Sciences Oversight Committee on Radioepidemiologic Tables (86). Briefly, if the ratios of baseline rates in the two populations vary markedly by age at diagnosis, it seems unlikely that both models can hold. In the case of breast cancer, baseline risk is about 4 times higher in the United States than in Japan, based on age-adjusted rates from the Connecticut, Miyagi Prefecture, and Nagasaki City tumor registries (82). On an age-specific basis, however, this ratio varies from less than 3 at ages under 50 to more than 6 at ages over 70. Thus, if the variation of baseline risk over time following some event, like a radiation exposure, is truly represented in both populations by the published population rates, and if within both populations the constant relative risk model holds, then, for an exposure at age 20 (say), estimates of average yearly absolute excess risk should not agree between Japanese and Americans both for the period 10-30 years after exposure and the period 40-60 years after exposure. Conversely, if measures of absolute risk agreed between the two populations for any similar follow-up period,

the distribution of excess risk over time should not follow the constant relative risk model in both populations. Yet the evidence which suggests that both models hold, or rather, that the two models are simultaneously consistent with epidemiological experience, was obtained largely from extensive follow-up data on breast cancer among Japanese atomic bomb survivors and North American populations exposed to medical X ray (49,50).

The apparent contradiction in the case of breast cancer would appear to have been resolved by Moolgavkar and Lee (87), who point out that published age-specific population cancer rates of the type cited above (e.g., from reference 82) are based on relatively short observation periods, and that rates for different ages at observation correspond to different birth cohorts. Moreover, they offer evidence that, within cohorts, the distribution of baseline breast cancer risk among Japanese women follows a common pattern, similar to that seen in western societies, but that the overall level of risk, at similar ages at observation, varies considerably by birth cohort. Breast cancer risk has steadily increased in Japan, and women born within the last 50 years or so are at higher risk than women born earlier. This trend is reflected in published population rates, which show proportionally lower risks at older ages because the women whose experience contributes to these rates are members of cohorts whose overall breast cancer risk is low. In the United States, on the other hand, breast cancer risk has been remarkably stable over at least the past 30 years (88), and therefore published age-specific rates are a better indication of the temporal distribution of baseline risk within a birth cohort. It should be noted that the analyses of Japanese atomic bomb survivor data, on which the inference of a constant relative risk over time after exposure is largely based, involved comparisons of cancer risk between heavily exposed and lightly exposed or nonexposed members of the same birth cohorts (5,48,49,50).

The above discussion demonstrates that no contradiction exists between the constant relative risk model for distribution in time and the constant absolute risk model for projection of risk from one population to another in the case of breast cancer. It does not demonstrate a similar lack of contradiction for all other cancers to which the models might be applied. In general, however, patterns of age-specific cancer risk do not differ between Japan and the United States to the same extent for such other cancers as they do for breast cancer (82), and it is therefore less likely for a contradiction between the two models to become apparent. To the extent that risk variation by age in the United States may reflect cohort effects, it would of course be preferable to apply the constant relative risk model, if appropriate, to cohort-specific baseline rates. That may be possible decades from now, when extensive cancer incidence data have been accumulated over many years, but it is not practicable at the present time.

Overall, the evidence favors absolute, as opposed to proportional transport of risk from one irradiated population to another. It should be noted, however, that the choice of the absolute model is based on data for only a few cancers and populations. For example, some population differences in cancer risk conceivably might depend upon differential exposure to an agent that interacts synergistically, or antagonistically, with radiation, and in such cases, the absolute model would not hold. As

with models for low-dose extrapolation of risk, the unresolved issues for extrapolation from one population to another involve questions fundamental to the nature of carcinogenesis.

REFERENCES – Chapter III

1. Upton, A. C., The Biological Effects of Low-Level Ionizing Radiation. Sci. Am. 246 (2): 41-49 (1982).

2. Jablon, S. and Bailer, J. C., The Contribution of Ionizing Radiation to Cancer Mortality in the United States. Prev. Med. 9: 219-222 (1980).

3. U.S. Department of Health and Human Services, "Cancer: The Health Consequences of Smoking: A Report from the Surgeon General." U.S. Government Printing Office, Washington, D.C., 1982.

4. Committee on the Biological Effects of Ionizing Radiation, "The Effects on Populations of Exposure to Low Levels of Ionizing Radiation: 1980." National Academy Press, Washington, D.C., 1980.

5. Kato, H. and Schull, W. J., Studies of the Mortality of A-Bomb Survivors. 7. Mortality, 1950-1978: Part 1. Cancer Mortality Radiat. Res. 90: 395-432 (1982).

6. United Nations Scientific Committee on the Effects of Atomic Radiation, "Sources and Effects of Ionizing Radiation." United Nations, New York, 1977 (Report E.77.IX.1).

7. ICRP Publication 26, Annals of the ICRP, "Recommendations of the International Commission on Radiological Protection." Pergamon Press, Oxford, 1977.

8. NCRP Report No. 38, "Protection against Neutron Radiation." National Council on Radiation Protection and Measurements, Washington, D.C. 1971.

9. Axelson, O., Edling, C., Kling, H., Andersson, L. and Ringner, A., Lung Cancer and Radon in Dwellings. Lancet 2: 995-996 (1981).

10. Stranden, E. and Berteig, L., Radon in Dwellings and Influencing Factors. Health Phys. 39: 275-284 (1980).

11. NCRP Report No. 77, "Exposure from the Uranium Series with Emphasis on Radon and its Daughters. National Council on Radiation Protection and Measurements, Washington, D.C., 1984.

12. NCRP Report No. 56, "Radiation Exposure from Consumer Products and Miscellaneous Sources." National Council on Radiation Protection and Measurements, Bethesda, MD, 1977.

13. Boice, J. D. and Land, C. E., Ionizing Radiation. In "Cancer Epidemiology and Prevention" (D. Schottenfeld and J. F. Fraumeni, Eds.), pp. 231-253 (1982).

14. Boice, J. D., Cancer Following Medical Irradiation. Cancer 47: 1081-1090 (1981).

15. Rowland, R. E., Stehney, A. F. and Lucas, H. F., Jr., Dose-response Relationships for Female Radium Dial Workers. Radiat. Res. 76: 368-383 (1978).

16. Archer, V. E., Gilliam, J. D. and Wagoner, J. K., Respiratory Disease Mortality Among Uranium Miners. Ann. New York Acad. Sci. 271: 380-293 (1976).

17. NCRP Report No. 78, "Occupational and Environmental Exposures to Radon and Radon Daughters in the United States." National Council on Radiation Protection and Measurements, Bethesda, MD, 1984.

18. Conard, R. A., Paglia, D. E., Larsen, P. R., et al., "Review of Medical Findings in a Marshallese Population Twenty-six Years after Accidental Exposure to Radioactive Fallout." BNL Report 51261. Brookhaven National Laboratory, Upton, New York, 1980.

19. Saenger, E. L., Thomas, G. E. and Tompkins, E. A., Incidence of Leukemia Following Treatment of Hyperthyroidism. J. Am. Med. Assoc. 205: 855-862 (1968).

20. Schull, W. J. and Kato, H., Malignancies and Exposure of the Young to Ionizing Radiation. Cancer Bull. 34: 88-89 (1982).

21. Ichimaru, M., Ishimaru, T. and Belsky, J. L., Incidence of Leukemia in Atomic Bomb Survivors Belonging to a Fixed Cohort in Hiroshima and Nagasaki, 1950-71. J. Radiat. Res. 19: 262-282 (1978).

22. Ichimaru, M., Ishimaru T., Mikami, M., Yamada, Y., and Ohkita, T., Incidence of Leukemia in a Fixed Cohort of Atomic Bomb Survivors and Controls, Hiroshima and Nagasaki, October 1950-December 1978. Technical Report 13-81, Hiroshima, Radiation Effects Research Foundation, 1981.

23. Tokunaga, M., Land, C. E., Yamamoto, T., Asano, M., Tokuoka, S., Ezaki, E., Nishimori, I. and Fujikura, T., Breast Cancer Among Atomic Bomb Survivors. In "Radiation Carcinogenesis: Epidemiology and Biological Significance" (J. D. Boice and J. F. Fraumeni, Jr., Eds.), pp. 45-56. Raven Press, New York, 1984.

24. Ishimaru, T., et al., Incidence of Thyroid Cancer among Atomic Bomb Survivors and Controls, Hiroshima and Nagasaki, 1958-1979: Relationship to Radiation Dose Absorbed by Thyroid Gland. Unpublished manuscript dated September 20, 1983.

25. Tokunaga, M., Land, C. E., Yamamoto, T., Asano, M., Tokuoka, S. Ezaki, H. and Nishimori, I., Breast Cancer in Japanese A-bomb Survivors. Lancet 2: 924 (1982).

26. Hildreth, M. G., Shore, R. E. and Hempelmann, L. H., Risk of Breast Cancer among Women Receiving Radiation Treatment in Infancy for Thymic Enlargement. Lancet 2: 273 (1983).

27.   MacMahon, B. and Hutchison, G. B., Prenatal X Ray and Childhood Cancer:
      A Review. *Acta Unio. Int. Contra Cancrum*, 20: 1172-1174 (1964).

28.   Totter, J. R. and MacPherson, H. G., Do Childhood Cancers Result
      from Prenatal X Rays? *Health Phys.* 40: 511-524 (1981).

29.   Monson, R. R. and MacMahon, B., Prenatal X-ray Exposure and Cancer
      in Children. In "Radiation Carcinogenesis: Epidemiology and
      Biological Significance" (J. D. Boice, Jr. and J. F. Fraumeni, Jr.,
      Eds.), pp. 97-105. Raven Press, New York, 1984.

30.   Hempelmann, L. H., Hall, W. J., Phillips, M., Cooper, R. A. and
      Ames, W. R., Neoplasms in Persons Treated with X-rays in Infancy:
      Fourth Survey in 20 Years. *J. Natl. Cancer Inst.* 55: 519-530 (1975).

31.   Jablon, S. and Kato, H., Childhood Cancer in Relation to Prenatal
      Exposure to Atomic-bomb Radiation. *Lancet* 2, 1000-1003 (1970).

32.   Kneale, G. W. and Stewart, A. M., Mantel-Haenszel Analysis of Oxford
      Data. I. Independent Effects of Several Birth Factors Including
      Fetal Irradiation. *J. Natl. Cancer Inst.* 56: 879-883 (1976).

33.   Mole, R. H., Antenatal Irradiation and Childhood Cancer: Causation
      or Coincidence? *Br. J. Cancer* 30: 100-208 (1974).

34.   Harvey, E. L., Prenatal X Ray and Childhood Cancer in Twins. Johns
      Hopkins Univ. Unpublished Doctoral Dissertation, 1983.

35.   Upton, A. C., Odell, T. T. and Sniffen, E. P., Influence of Age at
      Time of Irradiation on Induction of Leukemia and Ovarian Tumors
      in RF Mice. *Proc. Soc. Exp. Biol. Med.* 104: 769-772 (1960).

36.   Brent, R. L., Effects of Ionizing Radiation on Growth and Development.
      Controversies in Epidemiology and Biostatistics 1: 147-183 (1979).

37.   Sasaki, S., Kasuga, T., and Kawashima, N., Influence of Physical
      and Biological Factors on Radiation Carcinogenesis: Age-dependence
      of Susceptibility to Radiation Carcinogenesis. In "Final Report:
      Risks due to Low Level Radiation Exposures, Project Research in FY
      1973-1982." National Institute of Radiological Sciences (NIRS-M-47),
      Anagawa, Chiba, Japan, 1983.

38.   Sasaki, S., Tsutomu, K., Sato, F., and Kawashima, N., Late Effects
      of Fetal Mice Irradiated at Middle or Late Uterine Stage. *Gann*
      69: 167-177 (1978).

39.   Sasaki, S. and Kasuga, T., Life Shortening and Carcinogenesis in Mice
      Irradiated Neonatally with X Rays. *Radiat. Res.* 88: 313-325 (1981).

40.   Sasaki, S. and Kasuga, T., Life Shortening and Carcinogenesis in Mice
      Irradiated at the Perinatal Period with Gamma Rays. In "Proceedings
      of the 22nd Hanford Life Sciences Symposium, Richland, Washington,
      Sept. 27-29, 1983" (in press).

41. National Cancer Institute, "Surveillance, Epidemiology, and End Results. Incidence and Mortality Data: 1973-1977." NCI Monogr. 57, U. S. Govt. Printing Office, Washington, D.C., 1981.

42. Armenian, K. H. and Lilienfeld, A. M., The Distribution of Incubation Periods of Neoplastic Diseases. Am. J. Epidemiol. 99: 92-100 (1974).

43. Raventos, A. and Winship, T., The Latent Interval for Thyroid Cancer Following Irradiation. Radiology 83: 501-508 (1964).

44. Mayneord, W. V. The Time Factor in Carcinogenesis: The 1977 Sievert Lecture. Health Phys. 34: 297-309 (1978).

45. Sartwell, P. E., The Distribution of Incubation Periods of Infectious Disease. Am. J. Hyg. 51: 310-318 (1950).

46. Mays, C. W. and Spiess, H., Epidemiological Studies of German Patients with Ra-224. In: "Epidemiology Applied to Health Physics" (Proceedings of the Sixteenth Midyear Topical Meeting, Health Physics Society, Albuquerque, NM. January 9-13, 1983), pp. 159-166. National Technical Information Service CONF-830101.

47. Ichimaru, M. and Ishimaru, T. Leukemia and Related Disorders. J. Radiat. Res. 16 (Supplement): 89-96 (1975).

48. Land, C. E. and Norman, J. E., Latent Periods of Radiogenic Cancers Occurring among Japanese A-bomb Survivors. In: "Late Biological Effects of Ionizing Radiation", Vol. 1, pp. 29-47. International Atomic Energy Agency, Vienna, 1978.

49. Land, C. E. and Tokunaga, M., Induction Period. In "Radiation Carcinogenesis: Epidemiology and Biological Significance" (J. D. Boice, Jr. and J. Fraumeni, Jr., Eds.), pp. 421-436. Raven Press, New York, 1984.

50. Land, C. E., Boice, J. D., Jr., Shore, R. E., Norman, J. E. and Tokunaga, Breast Cancer Risk from Low-Dose Exposures to Ionizing Radiations: Results of Parallel Analysis of Three Exposed Populations of Women. J. Natl. Cancer Inst. 65: 353-376 (1980).

51. Land, C. E., personal communication.

52. Land, C. E., Extrapolation from Large-scale Radiation Exposure. In: "Assessment of Risk from Low-level Exposure to Radiation and Chemicals: A Critical Overview", in press.

53. Gofman, J. W., "Radiation and Human Health." Sierra Club Books, San Francisco, 1981.

54. Steel, G. G. "Growth Kinetics of Tumours." Clarendon Press, Oxford, 1977.

55. NCRP Report No. 64. "Influence of Dose and its Distribution in
     Time on Dose-response Relationships for Low-LET Radiations."
     National Council on Radiation Protection and Measurements,
     Washington, D.C., 1980.

56. Whittemore, A. and Keller, J. B., Quantitative Theories of
     Carcinogenesis. SIAM (Soc. Ind. Appl. Math.) Rev. 20: 1-30 (1978).

57. Brown, C. C., Fears, T. R., Gail, M. H. et al., Models for Carcino-
     genic Risk Assessment. Science 202: 1105-1109 (1978).

58. Crump, K. S., Dose Response Problems in Carcinogenesis. Biometrics
     35: 157-167 (1979).

59. Interagency Regulatory Liaison Group, Scientific Bases for Identifi-
     cation of Potential Carcinogens and Estimation of Risks. J. Natl.
     Cancer. Inst. 63: 241-268 (1979).

60. Fialkow, P. J., Clonal Origin and Stem Cell Evolution of Human
     Tumors. In: "Progress in Cancer Research and Therapy", Vol. 3:
     "Genetics of Human Cancer" (J. J. Mulvihill, R. W. Miller, and
     J. F. Fraumeni, Jr., Eds.), pp. 439-453. Raven Press, New York, 1977.

61. Cairns, N., The Origin of Human Cancers. Nature (London) 389:
     353-357 (1981).

62. Straus, D. S., Somatic Mutation, Cellular Differentiation, and
     Cancer Causation. J. Natl. Cancer Inst. 67: 233-241 (1981).

63. Upton, A. C., Role of DNA Damage in Radiation and Chemical Carcino-
     genesis. In "Environmental Mutagens and Carcinogens." Proceedings
     of the 3rd International Conference on Environmental Mutagens
     (R. Sugimura, S. Kondo and H. Takebe, Eds.), pp. 71-80. University of
     Tokyo Press, Tokyo/Alan R. Liss, Inc., New York, 1982.

64. Moolgavkar, S. H. and Knudson, A. G., Mutation and Cancer: A Model
     for Human Carcinogenesis. J. Natl. Cancer Inst. 66: 1037-1052 (1981).

65. Bartsch, H., Tomatis, L. and Malaveille, C., Qualitative and Quanti-
     tative Comparison between Mutagenic and Carcinogenic Activities of
     Chemicals. In "Mutagenicity": New Horizons in Genetic Toxicology"
     (J. A. Heddle, Ed.), pp. 35-72. Academic Press, New York, 1982.

66. Yunis, J. J., The Chromosomal Basis of Human Neoplasia. Science
     221: 227-236 (1983).

67. United Nations Scientific Committee on the Effects of Atomic Radiation,
     "Ionizing Radiation: Sources and Biological Effects." (Report to
     the General Assembly, with Annexes). United Nations, New York, 1982.
     (Report E.82.IX.8.)

68. Crump, K. S., Hoel, D., Langley, C. and Peto, R., Fundamental Carcino-
     genic Processes and Their Implications for Low Dose Risk Assessment.
     Cancer Res. 36: 2973-2979 (1976).

69. Peto, R., Carcinogenic Effects of Chronic Exposure to Very Low Levels of Toxic Substances. Environ. Health Perspect. 22: 155-159 (1978).

70. Van Ryzin, J., The Assessment of Low-Dose Carcinogenicity. Biometrics (Suppl.): "Current Topics in Biostatistics and Epidemiology", 130-139 (1982).

71. Land, C. E., Estimating Cancer Risks from Low Doses of Ionizing Radiation. Science 209: 1197-1203 (1980).

72. Tokunaga, M., Land, C. E., Yamamoto, T., Asano, M., Tokuoka, S., Ezaki, E. and Nishimori, I., Incidence of Female Breast Cancer Among Atomic Bomb Survivors, Hiroshima and Nagasaki, 1950-1980. RERF Technical Resport (in press).

73. Modan, B., Ron. E. and Werner, A., Thyroid Cancer Following Scalp Irradiation. Radiology 123: 741-744 (1977).

74. Brown, J. M., The Shape of the Dose-Response Curve for Radiation Carcinogenesis: Extrapolation to Low Doses. Radiat. Res. 71: 34-50 (1977).

75. Baverstock, K. F., Papworth, D. and Vannart, J., Risks of Radiation at Low Dose Rates. Lancet i: 430-433 (1981).

76. Smith, P. G. and Doll, R., Mortality among Patients with Ankylosing Spondylitis after a Single Treatment Course with X-Rays. Br. Med. J. 284: 449-460 (1982).

77. Boice, J. D., Day, N. E., Anderson, A. et al., Cancer Risk Following Radiotherapy of Cervical Cancer. In "Radiation Carcinogenesis: Epidemiology and Biological Significance" (J. D. Boice and J. F. Fraumeni, Jr., Eds.), pp. 161-180. Raven Press, New York, 1983.

78. Shore, R. E., Albert, R. E. and Pasternack, B. S., Follow-up Study of Patients Treated by X-ray Epilation for Tinea Capitis: Resurvey of Post-treatment Illness and Mortality Experience. Arch. Environ. Health 31: 17-24 (1976).

79. Whittemore, A. S. and McMillan, A., Lung Cancer Mortality among U.S. Uranium Miners: A Reappraisal. J. Natl. Cancer Inst. 71: 489-499 (1983).

80. Radford, E. P., and St. Clair Renard, K. G., Lung Cancer in Swedish Iron Miners Exposed to Low Doses of Radon Daughters. New Engl. J. Med. 310: 1485-1494 (1984).

81. Blot, W. J., Akiba, S. and Kato, H., Ionizing Radiation and Lung Cancer: A Review Including Preliminary Results from a Case-control Study among A-Bomb Survivors. In "Atomic Bomb Survivor Data: Utilization and Analysis" (R. L. Prentice and D. J. Thompson, Eds.), pp. 235-248. SIAM (Society for Industrial and Applied Mathematics), Philadelphia, 1984.

82. Waterhouse, J., Muir, C., Shanmugaratnam, K. and Powell, J.
    (Eds.), "Cancer Incidence in Five Continents," Vol. IV. Inter-
    national Agency for Research on Cancer, Lyon, 1982.

83. Land, C. E., Cancers of the Digestive Tract and Accessory Organs.
    In "Radiation Carcinogenesis" (A. C. Upton, R. E. Shore and R. E.
    Albert, Eds.), in press. Elsevier North-Holland, New York, 1985.

84. Darby, S. C., Nakashima, E. and Kato, H., Parallel Analysis of
    Cancer Mortality among Atomic Bomb Survivors and Patients with
    Ankylosing Spondylitis Given X-ray Therapy. RERF Technical
    Report, Hiroshima, Japan, Radiation Effects Research Foundation,
    in press.

85. Haenszel, W., Kurihara, M., Segi, M., et al., Stomach Cancer among
    Japanese in Hawaii. J. Natl. Cancer Inst. 49: 969-988 (1972).

86. Oversight Committee on Radioepidemiologic Tables, "Assigned Share
    for Radiation as a Cause of Cancer. Review of Radioepidemiologic
    Tables Assigning Probabilities of Causation." National Academy
    Press, Washington, D.C., 1984.

87. Moolgavkar, S. H. and Lee, J. A. H., Temporal Trends in Breast
    Cancer. Am. J. Epidemiol. 115:759-777 (1982).

88. Riggan, W. B., Van Bruggen, J., Acquavella, J. F., Beaubier, J.
    and Mason, T. J., "U.S. Cancer Mortality Rates and Trends, 1950-
    1979", Vol. II, U.S. Govt. Printing Office, Washington, D.C., 1983.
    [EPA-600/1-83-015b.]

Natural Sources :

Environmental
    Cosmic Radiation
    Terrestrial Radiation
    Internal Radioactive
    Isotopes

Manmade Sources :

Environmental
    Technologically Enhanced
    Global Fallout
    Nuclear Power
Medical
    Diagnostic
    Radiopharmaceuticals
Occupational
Consumer Products
    and Miscellaneous

Dose Per Year (Millirem)
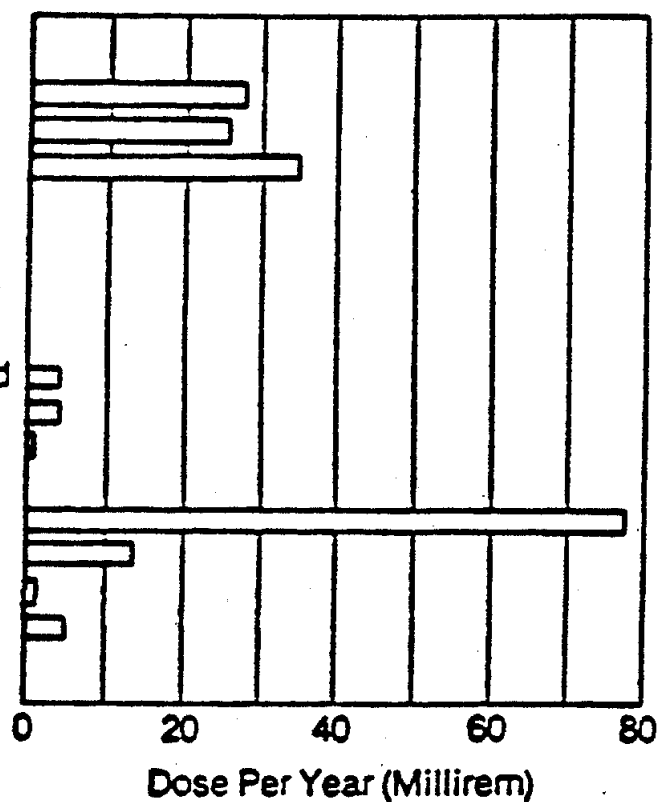
Figure III-1. Radiation exposure of a typical person in the U.S.
from natural and man-made sources. [Redrawn from ref. 1.]
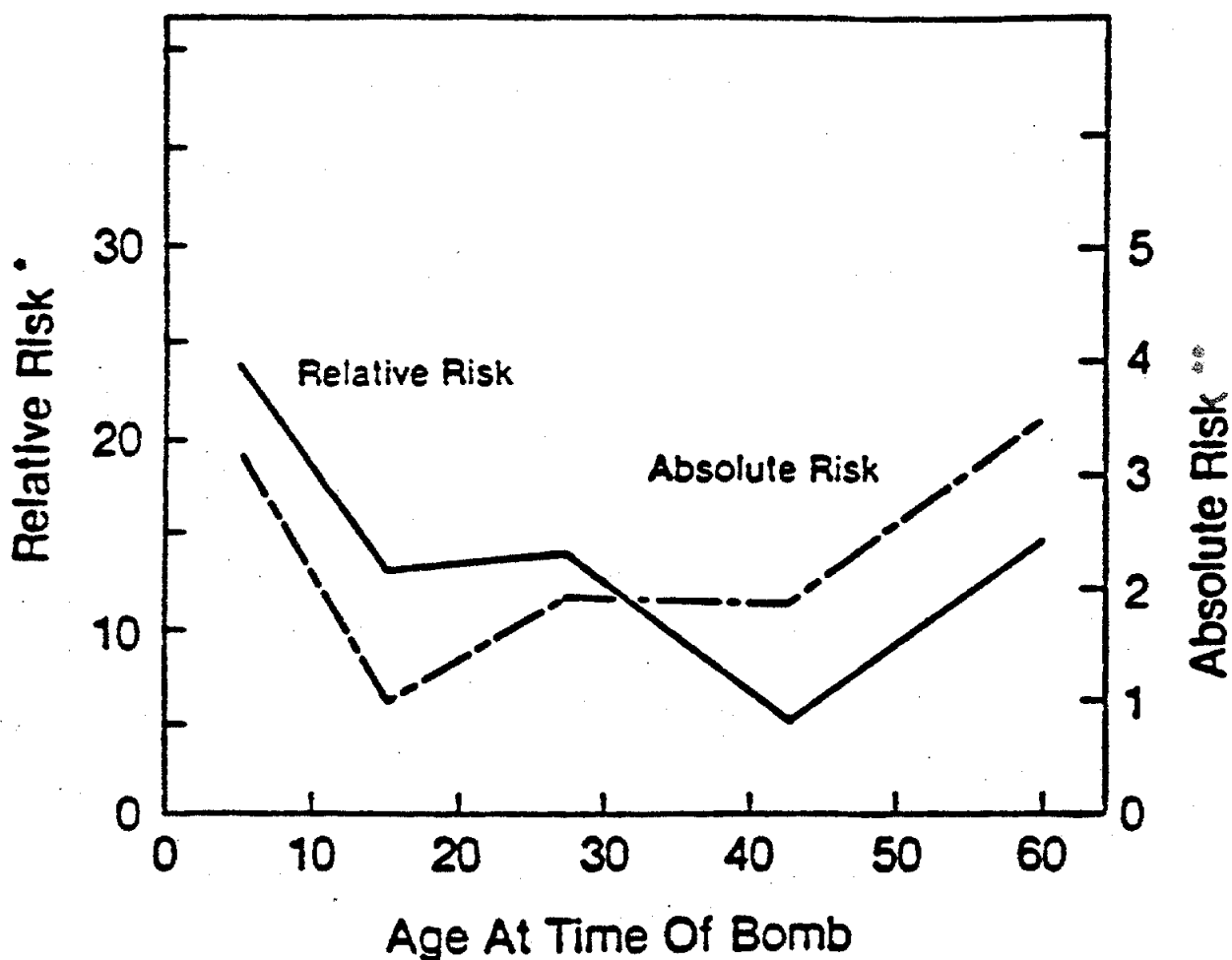
Figure III-2. Measures of leukemogenic effect among A-bomb survivors, by age at the time of the bomb, average for both cities.

The footnotes explaining the two ordinate scales are:

*Risk of 100+ versus 0-9 rad.

**Excess cancers per million persons per year per rad.

[Redrawn from Beebe, G. W., Kato, H., and Land, C. E., Radiat. Res. 75: 138-201 (1978), Fig. 1.]
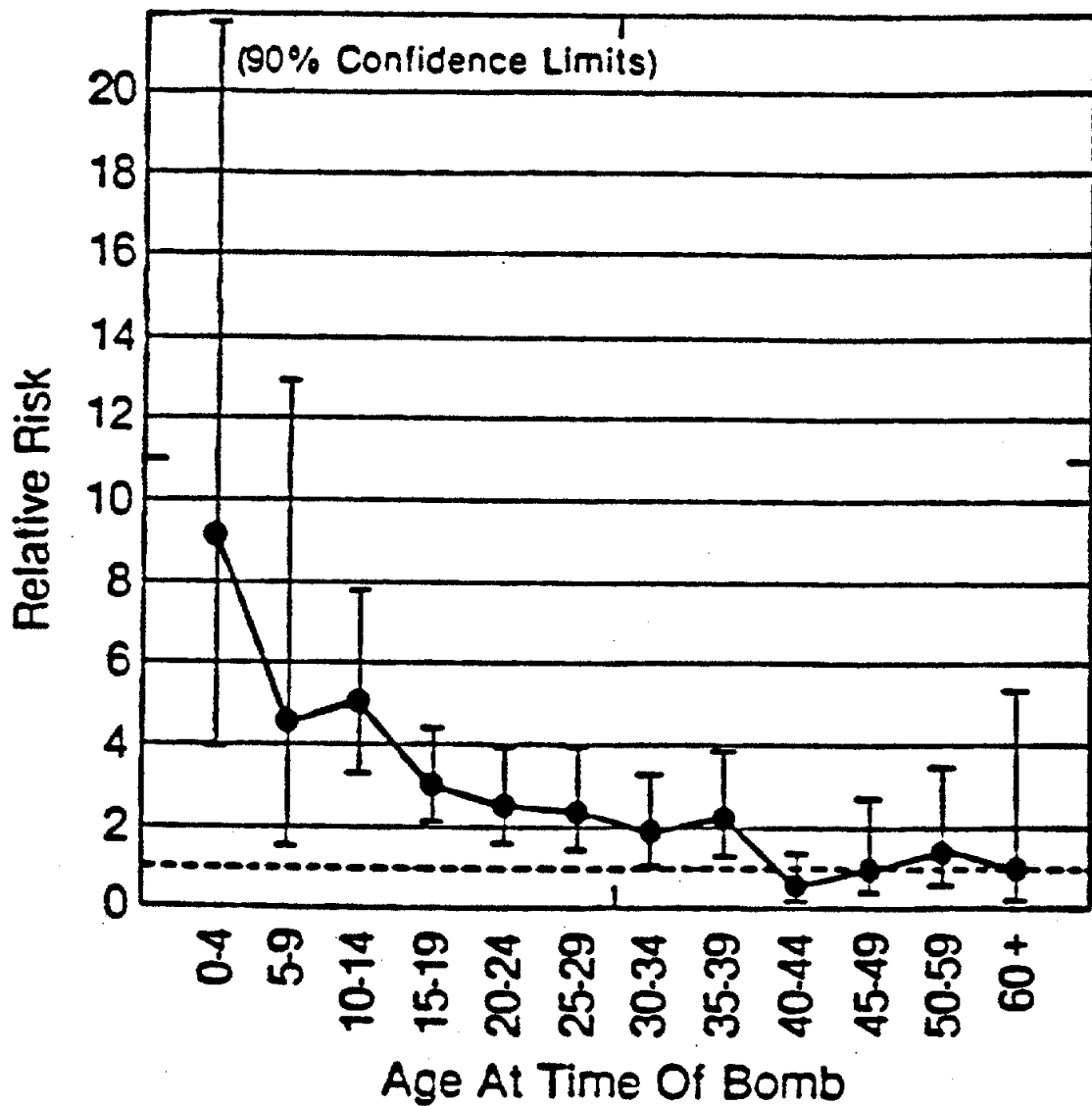
Figure III-3. Relative risk of breast cancer among female Japanese
A-bomb survivors, incidence 1950-1980, 50+ rad versus 0-9 rad and
non-exposed, by age at the time of the bombings, both cities combined.
[Land, C. E., unpublished data.]
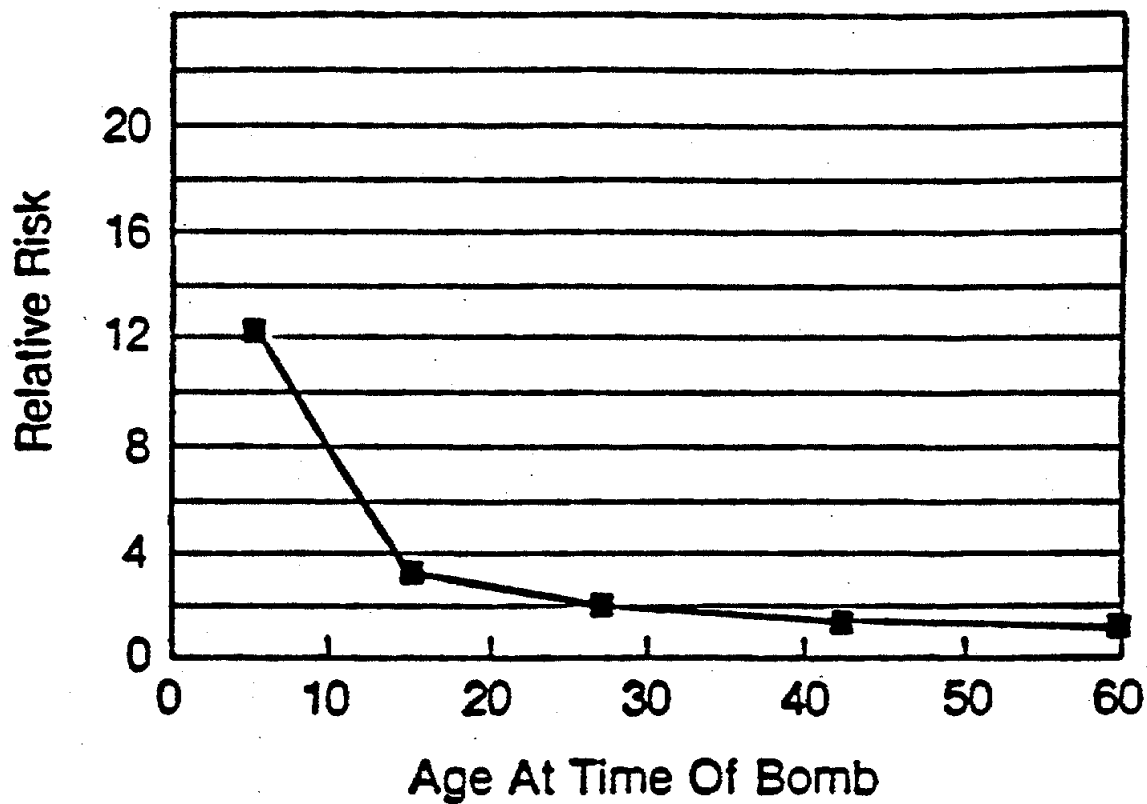
Figure III-4. Relative risk of all forms of cancer except leukemia
among Japanese A-bomb survivors, mortality 1950-1978, 200+ rad versus
under 1 rad, by age at the time of the bombings, both cities combined.
[Redrawn from Kato, H., and Schull, W. J., Radiat. Res. 90: 395-432
(1982), Fig. 4.]

Chapter IV: THE PROBABILITY OF CAUSATION

A. General

The word "probability" has a number of definitions, but even more protean is "cause" or "causation." We are satisfied that the "cause" of the light going on is the closing of the electric circuit. But what is the "cause" of a case of tuberculosis? The answer is usually "infection with the tubercle bacillus, of course." But the inhalation of a modest number of tubercle bacilli will be followed by clinical disease in only a minority of persons or experimental animals. Some individuals are more susceptible than others. Is the "cause" of clinical disease in a given person the bacillus or the susceptibility, or both? Those who consider this example strained might reflect that, 100 years ago, virtually everyone who lived in a crowded, poor, urban environment was infected by tubercle bacilli, yet only a minority contracted clinical disease. In some sense, in that situation, the "cause" of tuberculosis was susceptibility.

The above is preliminary to a definition of what we mean here by "probability of causation." We must define the term not only precisely, but so that it leads to a unique mathematical formulation that will govern the calculations required for the radioepidemiological tables. The definition that we give below is the operational definition for this expression. The definition carries with it certain implications, some of which reflect important policy decisions.

B. Definition

Let a particular possible outcome event be denoted C. Let X (a vector) denote the particular set of individual characteristics. Denote the presence of a possible cause by D and its absence by $\overline{D}$.

Then $P(C, D;X)$ is the probability of outcome C if D is present, conditional on the characteristics X. Similarly, $P(C, \overline{D};X)$ is the probability of outcome C if D is not present. Then D is a possible "cause" of C only if

$$P(C, D;X) > P(C, \overline{D};X).$$

Define $Ex(C, D;X) = P(C, D;X) - P(C, \overline{D};X).$

as the increase in the probability of C due to the presence of D. Then, the probability of causation of C by D, the PC, is <u>defined</u> as:

$$PC(C, D;X) = Ex(C, D;X)/P(C, D;X). \qquad (IV-1)$$

In words, the PC is defined as the increase in the probability of C due to D as a proportion of the probability of C given D, everything conditional on the characteristics X.

Note that the PC does not allocate causation as between characteristics X and Y. If, for example, the event C is the occurrence of lung

cancer, and if D is exposure of the lung to 20 rad of gamma radiation, while X and Y represent, respectively, being a regular cigarette smoker, or a non-smoker, then according to our definition, PC(C, D;X) measures the probability of causation of lung cancer from 20 rad among smokers and PC(C, D;Y) that among non-smokers.

Although it can be argued that cigarette smoking is a far more important cause of lung cancer than is ionizing radiation, our work addresses the radiation risk exclusively: Given a person, with whatever risk factors may apply to him, what is the probability that the documented radiation dose that he received was the "cause" of his cancer? This may be interpreted as: what proportion of his total risk resulted from the radiation? Although the question might be asked (and answered), we do not address "What proportion of the risk resulted from smoking?" or "What proportion arose from the combination of smoking and radiation?"

The phrase "Probability of Causation" is intuitively appealing, but the ratios so designated are not probabilities in a mathematically rigorous sense. It must be recognized that different persons vary as to their (prospective) chances of having cancer. Besides age and sex, other characteristics such as diet, exposures to carcinogenic chemicals, genetic factors and a host of others, some of which can only be guessed at, all combine to increase or decrease from the average value the chance that a specific person will contract a particular kind of cancer. For present purposes it is possible to take account of only a limited number of such characteristics, principally age, sex and cigarette smoking habit. The probabilities of cancer, then, are average values for all persons in a given class, for example, male non-smokers aged 35 years. The Probability of Causation that is calculated for an individual in that class will be more or less correct as his personal characteristics match or vary from the average in the class. Nevertheless, our procedure assigns the same PC to all members of the class.

Evidently, were the classes defined differently – for example, by specification of residence in Utah, the calculated PC might well change. In effect, our procedure partitions the population of the United States into a set of mutually exclusive classes, by sex, age and smoking charac-teristics. These characteristics were chosen because 1) they affect cancer rates in important ways which can be specified from available data, and 2) every person can be assigned unequivocally to one of the classes.

It has been suggested that the term "Assigned Share" would more accurately describe the ratios that are calculated (1). We are, however, constrained by the legislative mandate embodied in Public Law 97-414 wherein the specific term "Probability of Causation" is employed.

Although the PC as defined can be calculated prospectively, it would have little meaning for any person because of its specificity as to type of cancer and date of diagnosis, as well as tissue dose and age at exposure. Following the imposition of cause D, an individual may be interested in P(C, D;X) – "What is the probability that C will occur?" or in P(C, D;X) – P(C, $\overline{D}$;X) – "By how much has the probability that C will occur been increased?", but PC(C, D;X) tells him that if the event C does

occur, then PC(C, D;X) is the probability that D is the "cause" in the sense described above. In short, PC(C, D;X) will usually be of interest only retrospectively; supposing event C (a cancer) has occurred, what is the probability that D was the cause?

C. Specifics

The discussion above is purposely quite general. To be more specific:

The event C will be the occurrence (clinical detection) of a particular cancer that is known to be inducible by ionizing radiation and for which specific estimates of the risk from particular radiation doses can be made.

The cause D will be the receipt, by the organ in which the cancer has arisen, of a specified radiation dose.

The characteristics X of the person under consideration will include, at a minimum, the age at which the radiation was received, the number of years after radiation when the cancer was diagnosed and the sex of the individual.

We shall usually be concerned with annual rates of occurrence, the rate representing the yearly number of cases of C per 100,000 or per million persons.

The values $P(C, \overline{D};X)$ will be identified with the incidence rates provided by the SEER Program (2) for the years 1973-1981 for all areas, excluding Puerto Rico. Although, formally, an incidence rate is not a probability, the numerical difference is trivial over any interval for which the probability of death from all causes is small. We shall refer to these rates as the "Baseline Rates."

D. Calculational Formulas

There is a calculational advantage in expressing the PC in terms of the relative excess risk R = R(C, D;X), defined as the increase due to D as a proportion of the probability of C in the absence of D:

$$R(C, D;X) = Ex(C,D;X)/P(C, \overline{D};X).$$

Writing P(C,D;X) as the sum of Ex(C,D;X) and $P(C, \overline{D};X)$ and dividing both the numerator and denominator in (IV-1) by $P(C, \overline{D};X)$, we obtain

$$PC(C,D;X) = R(C,D;X)/(1 + R(C,D;X)). \qquad (IV-2)$$

The advantage of expressing the PC in terms of R is that R is the simple product of several quantities that are naturally thought of separately, and that can be either calculated using simple formulae or presented in tables. For example, in Chapter X, Section 10, we find that the relative excess of breast cancer following exposure to radiation

is proportional to dose and that, for a single exposure to low-LET radia-
tion at age 15, the relative excess for a typical American woman is .0107
times dose in rad, at any time more than 10 years after exposure (Table
X-10). If a cancer should be diagnosed at age 37, for example, following
exposure at age 15 to 30 rad, the relative excess would be R(breast cancer,
30 rad;age 15, 22 years) = (30)(.0107) = 0.321, and the PC would be
0.321/1.321 = .243 or 24%.

E. Cases in which US Baseline Incidence Does not Apply

PC calculations based on SEER values for baseline cancer incidence
require the assumption that the individual in whom cancer was diagnosed
following a documented radiation exposure would have been, in the absence
of that exposure, "typical" of the US population for his or her age and
sex with respect to cancer risk. But the subject may have had an atypical
history of exposure (or nonexposure) to known carcinogens or may have ex-
perienced other life events associated with a higher or lower cancer risk
than average. Or the subject may be a member, perhaps even a "typical"
member, of an ethnic, religious, or other population subgroup known to
have cancer rates higher or lower than the U.S. population as a whole.
Should the PC calculations be modified in such cases, and if so, how?

Having introduced the problem, we should also make it clear that it
is a problem about which very little is known. Although experimental
studies have demonstrated that levels of carcinogenic response to ionizing
radiation can be modified drastically through the use of certain so-called
"promoters", agents that do not in themselves appear to initiate the car-
cinogenic process, we do not know whether or not similar agents contri-
bute to human cancer risk associated with radiation. It is by no means
clear, at this time, whether people who are at high risk of cancer in the
absence of radiation exposure are more sensitive than other people to the
carcinogenic effects of radiation. Epidemiological research in the area
of combined effects of different risk factors is difficult because combin-
ations that might be of interest are relatively rare, and in the case of
radiation and other factors, such epidemiological study is just beginning.

The estimates of cancer risk from radiation exposure presented by
the BEIR III Committee were based on syntheses of data from various ex-
posed populations, some of which, like the Japanese A-bomb survivors,
have cancer incidence levels for certain cancer sites that are very
different from U.S. rates. Making the estimates involved the implicit
assumption that the carcinogenic effects of radiation are additive with
respect to whatever factors are responsible for differences between
population cancer rates. This assumption appears to hold for breast
cancer in the case of Japanese and American women (3), for whom population
rates differ by a factor of 4 or 5, and it is not inconsistent with data
on radiation-induced stomach cancer in A-bomb survivors and British
patients treated with X radiation for ankylosing spondylitis (4). There
may be other sites for which the assumption does not hold, but we have no
way of knowing at present.

Clearly, the problem of calculating PC values in the presence of dif-
ferences in total cancer incidence because of exposure to other carcinogenic

agents, personal history with respect to factors related to cancer risk, or membership in a particular population subgroup, is fraught with uncertainty. The problem is not difficult given certain assumptions, as illustrated in subsequent sections, but with very few exceptions the informational basis for such assumptions is lacking. Without such information, any rule for making use of additional cancer data is necessarily arbitrary, and it may be preferable simply to proceed as if the subject were a typical member of the U.S. population.

F. Multiple Radiation Exposures

If two radiation exposures to doses D_1 and D_2, respectively, would, if given alone, result in excess risks $E(D_1)$ and $E(D_2)$ at an age for which the baseline risk is I, and if they are separated in time by a day or more so that they do not interact, it is assumed that the excess from the two exposures is the sum of the respective excesses, $E(D_1,D_2) = E(D_1) + E(D_2)$. The relative excess for the two exposures, $R(D_1,D_2) = E(D_1,D_2)/I$, is therefore the sum of the separate relative excesses, each computed as if only one had occurred:

$$R(D_1,D_2) = E(D_1,D_2)/I = E(D_1)/I + E(D_2)/I = R(D_1) + R(D_2).$$

Clearly, a PC calculation should be based on both the exposures or, if only one is of interest (perhaps one was voluntary and the other involuntary), the calculation should take account of the fact that the total risk was altered by the other exposure. If the first exposure is the one of interest, the calculated relative excess should take account of that by replacing I with

$$I' = I \times (1 + R(D_2)).$$

It will be convenient to write $W(D_2) = 1/(1 + R(D_2))$, so that $I/I' = W(D_2)$. The relative excess for the first exposure given the second then is

$$R(D_1;D_2) = (E(D_1,D_2)-E(D_2))/I' = E(D_1)/I' = R(D_1) \times W(D_2). \qquad (IV-2)$$

The role of $W(D_2)$, therefore, is to put the relative excess due to D_1 in the context of the baseline risk as altered by D_2. The PC value for the first exposure given the second is

$$PC(D_1;D_2) = R(D_1;D_2)/(1+ R(D_1;D_2)) = (R(D_1)W(D_2))/(1+R(D_1)W(D_2)),$$

a number different from and, in this example, smaller than the value $PC(D_1)$ which would have resulted if the second exposure had not taken place.

G. Modification of the PC Formula To Take Account of the Effects of Exposure to Carcinogens Other Than Radiation

A person with a malignant neoplasm of a kind that can be induced by radiation may have a history not only of radiation exposure, but also of exposure to other carcinogens that may be significant with respect to that particular cancer. Cigarette smoking or benzene exposure are examples. The PC has been defined as being conditional upon individual characteristics,

among which are included other carcinogenic exposures, but it may vary
depending on the presence (or absence) of exposure to other carcinogens.

It is not possible to modify the PC formula to account for every
possible exposure that can be listed. For example, prolonged exposure to
inhaled asbestos fibers is a risk factor for lung cancer and for mesothe-
lioma. Although mesothelioma has not been shown definitely to be induced
by ionizing radiation, lung cancer has. If possible, therefore, it would
be desirable to take explicit account of the possible role of asbestos
exposure in the causation of a lung cancer in, for example, a shipyard
worker who had radiation exposures while working as a radiographer examin-
ing welds, who also had spent several years installing asbestos insulation,
and who smoked two packs of cigarettes daily. It is impossible to undertake
so complete an analysis at this time, because data concerning such combined
exposures are not available, and further because we are not yet able to
classify asbestos exposures adequately with respect to lung cancer risk
in relation to duration and intensity of exposure or exact type or fiber
size of mineral.

Models

The way in which exposure to another carcinogen affects the PC
depends upon the magnitude of the carcinogenic effect of that factor in
the presence or absence of radiation. Although the interaction between
the two factors might, theoretically, be extremely complex (even anta-
gonism might occur), two interaction modes are especially simple and
natural, and we confine our further attention to them. Those modes are
the multiplicative and the additive. We avoid using the term "synergism"
because it has been used by different writers with somewhat different
meanings, although some have defined it to mean what we call multiplicative
interaction and others as more than additive interaction.

(1) The Additive Interaction Model (AIM)

If the total excess risk from a radiation exposure and from another
risk factor is assumed to be the sum of the excess risks from each of the
two taken separately, we say that they interact additively. This is what
was assumed (on the basis of extensive information) for two radiation
exposures in section F above. As in that section, if $R(D)$ denotes the
relative excess for radiation at dose D and $R(Z)$, the relative excess for
another factor at level Z, the relative excess for both factors combined
is

$$R(D,Z) = R(D) + R(Z).$$

Defining, in continuing analogy with section F, the altered baseline due
to Z as

$$I' = I \times (1+R(Z)) = I/W(Z),$$

the relative excess for radiation given the other factor is

$$R(D;Z) = (E(D,Z)-E(Z))/I' = (R(D,Z)-R(Z)) \times W(Z) = R(D) \times W(Z). \quad (IV-3)$$

- 47 -

The PC for radiation given the other factor is

$$PC(D;Z) = R(D;Z)/(1+R(D;Z)) = (R(D) \times W(Z))/(1 + R(D) \times W(Z)).$$

(2)   The Multiplicative Interaction Model (MIM)

If the relative risk (the relative excess plus one) due to two risk factors is the product of the relative risks for the two factors taken separately, we say the two factors interact multiplicatively. Thus, if radiation interacts multiplicatively with another factor, the relative excess for radiation at dose D and the other factor at level Z is

$$R(D,Z) = (1 + R(D)) \times (1 + R(Z)) - 1,$$

and the relative excess for D given Z is

$$R(D;Z) = (E(D,Z)-E(Z))/I' = (R(D,Z)-R(Z)) \times W(Z)$$

$$= R(D) \times (1+R(Z)) \times W(Z) = R(D),$$

$$\text{and } PC(D;Z) = PC(D).$$

H.   Cigarette Smoking and Lung Cancer

The most important risk factor which may be confounded with radiation in the causation of cancer is cigarette smoking, especially in relation to cancer of the lung and bronchus.

As has been shown, if a multiplicative interaction holds then the PC's for radiation causation do not vary according to the smoking history (nor would the PC's for smoking history vary according to the radiation history). Whittemore and McMillen (5) concluded that in a group of nearly 3,400 uranium miners, an MIM appeared to hold as between exposure to radon measured in cumulative Working Level Months and cigarette smoking measured as accumulated pack-years (one pack-year is one year's experience smoking one pack daily).

On the other hand, Prentice et al. (6) found that in a group of more than 40,000 residents of Hiroshima and Nagasaki, some of whom were exposed to a wide range of acute doses of radiation from the atomic bombs in those cities, the MIM definitely did not hold for death from all non-hematologic cancers and, specifically for lung cancer, the AIM fit the data better than the MIM.

Further, Blot et al. (7), in a case-control study of lung cancer in Hiroshima and Nagasaki have demonstrated that radiation and smoking inter- act in an additive way in the causation of lung cancer.

It is possible that the difference in results obtained by the several groups stems from an intrinsic difference between a radiation dose of sparsely ionizing radiation (gamma rays) received in a matter of seconds (A-bomb) and a dose of densely ionizing radiation (alpha-particle-

emitting radon daughters) received over a period of years. In any case, we will illustrate the calculations appropriate to the AIM.

(1) The Additive Interaction Model for Cigarette Smoking
and Lung Cancer.

The AIM formula (see Chapter IV-G) for a given level s of smoking is:

$$R(D;s) = R(D) \times W(s)$$

where

$$W(s) = 1/(1 + R(s)), \qquad \text{(IV-4)}$$

and where $R(s)$ represents the relative excess for smoking levels as compared to baseline lung cancer incidence.

Baseline incidence depends upon age; however, from Kahn's data (8), it is evident that $R(s)$ can be treated as independent of age. Because baseline incidence corresponds to the general population of smokers and nonsmokers, $R(s)$ is negative for smoking levels s corresponding to lung cancer risks less than average, such as nonsmoking, and the average over all levels of $R(s)$ is zero. Thus, if $p(0)$, $p(1)$,...,$p(k)$ is the distribution of the general population over integer values of s from $s = 0$ for nonsmokers to $s = k$ for heavy smokers,

$$p(0)(1+R(0))+...+p(k)(1+R(k)) = 1. \qquad \text{(IV-5)}$$

Published values of the relative risk $RR(s)$ of lung cancer at various smoking levels compare the rate at each level to that among nonsmokers, and can therefore be written as

$$RR(s) = (1+R(s))/(1+R(0)). \qquad \text{(IV-6)}$$

Therefore equation (IV-5) can be rewritten as

$$p(0) + p(1)RR(1)+...+p(k)RR(k) = 1/(1+R(0)) = W(0). \qquad \text{(IV-7)}$$

If the values $p(s)$ and $RR(s)$ are known then $W(0)$ can be calculated from IV-7 and $W(s)$ can be calculated from $W(0)$, IV-6, and IV-4 for $s = 1,2,...,k$ as $W(s) = W(0)/RR(s)$. $\qquad$ (IV-8)

The data on incidence of lung cancer used here refer to the period 1973-1981; we use data concerning smoking habits for the year July, 1964 – June, 1965 published by the National Center for Health Statistics (9). Since the SEER incidence data for the years 1973-1981 center on the year 1977, we apply the smoking percentages obtained in 1964-1965 to the incidence rates at ages ten years later; that is, for example, we apply the percentages obtained in 1964-1965 at ages 25-44 to incidence data for ages 35-54.

We copy the values of RR(s) from Rogot and Murray (10).

Text Table A

	RR(s)	p(s)* Males	p(s)* Females
Nonsmokers	1.00	29.82	59.01
Former smokers**	3.97	19.23	7.81
Present cigarette smokers – all	11.28	50.95	33.18
Present amount***			
<10/day	3.89	13.56	13.50
10–20/day	9.63	24.72	15.02
21–39/day	16.70	11.24	4.37
40+/day	23.70	1.43	0.30

*NCHS 10-34 shows a small number (3.3 percent of male smokers and 1.6 percent of female smokers) of unknown present amount; we have distributed these proportionately to the categories of known amount.

**The value of W for former smokers applies to persons who stopped smoking cigarettes at least five years prior to onset of lung cancer. The data of Rogot and Murray (10) show that during the first five years after cessation of smoking, the risk of death from lung cancer is actually more than one and one-half times that of current smokers, implying that some stop smoking because of early symptoms of what eventually will prove to be lung cancer. It seems most appropriate to treat such persons as if they were current cigarette smokers.

***The class intervals shown here are those used by Rogot and Murray (10); the NCHS 10-34 intervals are slightly different; less than 11; 11-20; 21-40; 41 and over.

From equation IV-7 we obtain:

Males $.2982 + 3.97 \times .1923 + 11.28 \times .5095 = 1/(1+R(0))$

Females $.5901 + 3.97 \times .0781 + 11.28 \times .3318 = 1/(1+R(0))$

so that

Males $W(0) = 1/0.1469$

Females $W(0) = 1/0.2154,$

whence, from equation IV-8 we obtain the values of $W(s)$.

<center>Values of W(s) - Lung Cancer</center>

Smoking Category	Males	Females
Total	1.00	1.00
Nonsmokers	6.81	4.64
Former smokers	1.71	1.17
Present cigarette smokers – all	0.604	0.411
<10/day	1.75	1.19
10-20/day	.707	.482
21-39/day	.408	.278
40+/day	.287	.196

---

(2) Probability of Causation for Lung Cancer – Additive
       Interaction Model.

Referring back to equation IV-2, it is evident that the smoking characteristic can be accounted for in calculating the PC merely by multiplying R(D) by the appropriate value of W(s). This process is exemplified, and illustrative examples are given, in Chapter X-9.

I. Subpopulations with Non-standard Cancer Risks

From a reading of SEER rates for the different reporting areas, it is easy to select examples in which cancer incidence for a particular reporting region, and especially a particular ethnic group within a particular reporting region, is markedly higher or lower than the rates used for this report, which were based on all reporting regions except

Puerto Rico. Presumably, these differences are due to differential exposures, and an individual case probably should be evaluated in terms of that individual's exposure history rather than in terms of regional or ethnic classification. For example, male lung cancer rates in Utah are about half as high as those in the United States as a whole, but this is ascribable to the fact that the proportion of smokers in Utah is smaller than that in the rest of the country, due to the predominance of the Mormon Church, which proscribes tobacco use among its members. As we have seen above, nonsmokers have less than one sixth the lung cancer rate among males generally. Clearly, for lung cancer, information about smoking is more useful than information about area of residence and, presumably, about other factors as well (i.e., a member of the Mormon Church who smokes is unlikely to have a lung cancer risk much different from that of a non-Mormon with the same smoking history).

As a purely calculational exercise, it is a simple matter to define a factor W for membership in a certain subpopulation, as the ratio of the appropriate SEER rate to the corresponding subpopulation rate. Whether this should, or can, be done, however, is another matter. Differences between subpopulations with respect to cancer rates may depend mainly upon differences in exposure histories, and except for exposure to tobacco smoke, in the case of lung cancer, and radiation exposures other than the one(s) of interest, there appears to be no basis for a model by which other exposures may interact with a radiation exposure of interest. Simply ignoring information about a possibly altered cancer rate, on the other hand, amounts to treating the factors responsible as if they were known to interact multiplicatively with radiation.

Although in the abstract it would be desirable to take account of factors that interact additively in the appropriate way, we are ignorant of the nature of interactions except for smoking and lung cancer. Moreover, even if one wished to take account of a particular interaction as if it were additive, the necessary data that would enable the calculations are not available. However, the relative risk time-response model for radiation is consistent with existing data, and also with the idea that many, if not all, other risk factors do interact multiplicatively with radiation. It should be recognized, however, that to use the tables ignoring the influence of any particular other factor, is equivalent to treating that factor as one that interacts multiplicatively with radiation.

REFERENCES - Chapter IV

1. Oversight Committee on Radioepidemiological Tables, "Assigned Share for Radiation as a Cause of Cancer, Review of Radioepidemiolgic Tables Assigning Probabilities of Causation" (Final Report). National Academy Press, Washington, D.C., 1984.

2. Young, J. L., Jr., Percy, C. L., and Asire, A. J. (Eds.), "Surveillance, Epidemiology, and End Results: Incidence and Mortality Data, 1973-1977." National Cancer Institute Monograph 57. NIH Publ. No. 81-2330. U.S. Government Printing Office, Washington, D.C., 1981.

3. Land, C. E., Boice, J. D., Jr., Shore, R. E., Norman, J. E., and Tokunaga, M., Breast Cancer Risk from Low-dose Exposures to Ionizing Radiation: Results of Parallel Analysis of Three Exposed Populations of Women. J. Natl. Cancer Inst. 65: 353-376 (1980).

4. Smith, P. G. and Doll, R., Mortality among Patients with Ankylosing Spondylitis after a Single Treatment Course with X Ray. Br. Med. J. 284: 449-460 (1982).

5. Whittemore, A. S. and McMillan, A., Lung Cancer Mortality among U.S. Uranium Miners. J. Natl. Cancer Inst. 71: 489-499 (1983).

6. Prentice, R. L., Yoshimoto, Y. and Mason, M. W., Relationship of Cigarette Smoking and Radiation Exposure to Cancer Mortality in Hiroshima and Nagasaki. J. Natl. Cancer Inst. 70: 611-621 (1983).

7. Blot, W. J., Akiba, S. and Kato, H., Ionizing Radiation and Lung Cancer: A Review Including Preliminary Results from a Case-Control Study among A-Bomb Survivors. In "Atomic Bomb Survivor Data: Utilization and Analysis" (R. L. Prentice and D. J. Thompson, Eds.), pp. 235-248. SIAM (Society for Industrial and Applied Mathematics), Philadelphia, 1984.

8. Kahn. H. A., The Dorn Study of Smoking and Mortality among U.S. In: "Epidemiological Approaches to the Study of Cancer and other Chronic Diseases" (W. Haenszel, Ed.), pp. 1-125. Natl. Cancer Inst. Monograph No. 19, U.S. Government Printing Office, Washington, D.C., 1966.

9. National Center for Health Statistics, "Cigarette Smoking and Health Care Characteristics, U.S., July 1964-June 1965." Series 10, No. 34, U.S. Department of Health, Education and Welfare, Washington, D.C., 1967.

10. Rogot, E. and Murray, J. L., Smoking and Causes of Death among U.S. Veterans: 16 Years of Observation. Public Health Rep. 95: 213-222 (1980).

CHAPTER V: DATA SOURCES, ASSUMPTIONS, AND MODELS

A.   Data Sources

The calculation of probabilities of causation for radiogenic cancers requires baseline data for individual cancers and parallel quantitative risk estimates for cancer arising from exposure to ionizing radiation. Although the bulk of the data on the risk of cancer is in the form of mortality rates, in the late 1930s the National Cancer Institute began periodic surveys of cancer incidence and survival. As the Surveillance, Epidemiology, and End Results (SEER) program, this effort, covering about 10 percent of the U.S population, now provides systematic, national incidence data for the period beginning with 1973 that are unequivocally the best source of data on cancer incidence for the U.S. Data for 1973-77 are published (1); the Working Group has had access to the unpublished tabulations through 1981 (Table V-1). Site-specific baseline incidence data by age and sex have been used here as the basis for PC calculations without regard to ethnic or geographic sources of variation that often are considerable. ·PC estimates are necessarily sensitive to the baseline incidence used in the calculation of relative excess risk, and choices must be made whenever incidence is known to vary with characteristics of individuals for whom such estimates are required. Although the SEER data extend to geographic and ethnic variation, there is some uncertainty about the statistical stability of much of this variation, and the extent to which it may reflect the influences of factors whose interaction with radiation in the causation of cancer is simply unknown. With the single exception of smoking related to lung cancer, the methods and calculations presented here are appropriate to "average" Americans whose baseline risk levels are represented by the combined SEER registries.

The use of a single set of rates also takes no account of changes in population incidence over time, but these have been considerable only for stomach cancer and lung cancer.

The PC calculations have been limited to sites and types of cancer for which radiation is known to be a cause and for which reasonable data exist for purposes of calculation. (See chapters VII and X for further discussion). Site-specific estimates of radiation-induced cancer risk in terms of incidence have been taken from Tables V-14 and V-16 of the 1980 BEIR report (2) with updating for several sites and with deletions appropriate to the calculation of PC values (Table V-2). The BEIR report is the only comprehensive source of human, site-specific incidence data relating radiation exposure to cancer risk and the time constraints placed upon the Working Group have precluded any systematic reworking of the relevant literature, much less the original data upon which it is based.

The A-bomb survivor data for leukemia (3) were subdivided by type to develop separate sets of risk estimates for acute leukemia and chronic granulocytic leukemia. The BEIR leukemia coefficients themselves were modified to achieve a more stable, and plausible, dependence of risk on age at exposure (see Section D, below). The lung cancer coefficients were revised on the basis of new data from the A-bomb survivor series (4) (see Chapter X-9). Recent reports of thyroid cancer and breast cancer

incidence among A-bomb survivors (5,6) provided new information on the dependence of risk on age at exposure, an issue that had not been resolved satisfactorily by the BEIR III Committee (see Section D). A recent review of studies of salivary gland cancer following childhood irradiation (7) provided a numerical risk estimate for exposure ages 0-14, and the site was included in the calculations. Finally, BEIR estimates for certain sites and exposure ages were evaluated and rejected as uncertain, and corresponding PC calculations were not performed. Of the 78 age, sex, and site-specific risk coefficients employed in the present report, 40 were taken directly from the BEIR report and 38 were taken from more recent sources; also other coefficients presented in the BEIR report for the lymphomas and "miscellaneous other" sites were not used (see Chapter VII-F).

B. Dose-Response and Dose-Rate-Effect Models

As discussed in Chapter III-H, the weight of radiobiological evidence favors a linear-quadratic dose response to low-LET radiation for most cancers, with a "crossover" dose, at which the components of risk proportional to dose and dose-squared are equal, somewhere between 50 and 200 rad (8). In general, the epidemiological evidence discriminates poorly among competing dose-response models (9). Thyroid cancer and female breast cancer are exceptional in that the epidemiological data strongly favor linearity (2,5,6). Accordingly, the Working Group has adopted linearity for breast and thyroid cancer and the BEIR III linear-quadratic model for all other sites, for PC calculations involving exposure to low-LET radiation. The BEIR III linear-quadratic model estimates excess cancer risk, following a radiation exposure of short duration, as

$$\text{Excess} = e_{LQ} \times (D + D^2/116),$$

where e_{LQ} is a site-specific coefficient depending upon age at exposure and sex, and D is radiation dose in rad (see Chapter III-H). The linear model, of course, expresses excess risk as

$$\text{Excess} = e_L \times D.$$

The so-called crossover dose of 116 rad in the formulation of the BEIR linear-quadratic model, which specifies the degree of curvature in the graph of risk as a function of dose, was originally determined from the Japanese leukemia data (2,3), but is also consistent with a number of other radiobiologic end points (see Chapter III-I). Since no other human cancer data are adequate for calculating crossover doses for individual sites other than the thyroid gland and female breast, the value of 116 rad has been assumed to apply to all sites for which a linear-quadratic dose-response model for low-LET radiation is considered appropriate for low-LET radiation (i.e., all cancers other than those of the thyroid and female breast).

Although the BEIR Committee's site-specific incidence risk coefficients, except for leukemia, corresponded to the linear dose-response model, the Committee provided numerical coefficients for both linear and

linear-quadratic models with respect to total mortality from all types of cancer other than leukemia, considered as a group (reference 2, Tables V-19 and V-20). The ratio of these coefficients,

$$e_L/e_{LQ} = 3.470/1.397 = 2.48 = 2.5,$$

and the crossover dose of 116 rad were used by the Working Group to convert the BEIR III linear-model coefficients to the corresponding linear-quadratic coefficients for the appropriate sites.

The present radioepidemiological tables have been prepared primarily for low-LET radiation exposures. The tables and algorithms may, however, be applied to high-LET radiation exposures by substituting for dose the "biologically equivalent dose" (BED) determined for the particular exposure. This calculation involves the assumption that for high-LET radiation the dose-response relationship is approximately linear, which may be justified for doses below 10 rad. In its simplest form, the BED is the product of the dose in rad and a "relative biological effectiveness" (RBE) factor for the given radiation (see Chapter III-B). The RBE factor depends on the end point selected and varies with the dose and with the LET of the radiation, which is a function not only of the energy of the incident radiation but also of the attenuation and scatter in the tissues surrounding the target tissue. For internally deposited radionuclides, estimates of equivalent doses are further complicated by spatial and temporal variations in the distribution of the sources of radiation. Therefore for a best estimate of the cancer risk from a given exposure to high-LET radiation, biologically equivalent doses must be calculated on a case-by-case basis, and it clearly would make little sense to produce separate PC tables for any given high-LET radiation. Exposure of bone to high-LET radiation from internally deposited radium-224 and lung exposures from radon daughters are a special case since since there is a direct observational basis for risk estimation (see Chapter X-2 and X-9).

The calculation of BED is a complicated process, and particularly so for radiation from internally deposited radionuclides. The Ad Hoc Working Group has made no attempt to pursue the issue beyond this point.

Considerations of dose rate and dose-fractionation effects influenced the Working Group's choice of the linear-quadratic model for cancer sites other than the breast and thyroid (see Chapter III-I). By treating exposures widely separated in time as independent, and therefore additive in effect, a model-dependent approach to dose rate was obtained. The scientific basis for this procedure is that repair of DNA sublesions is rapid, generally occurring within hours following irradiation. Consider a case in which exposures to D_1 and D_2 rad occurred during successive months. Under the linear model, the effects of the two exposures are proportional to D_1 and D_2, respectively, and their combined effect is therefore proportional to $D_1 + D_2$, just as if the two exposures had occurred simultaneously. Thus for fast neutrons and alpha particles in the lower-dose range (below 10 rad), and for low-LET radiation in the case of breast cancer or thyroid cancer, there is no reduction in effect due to fractionation or protraction of exposure. Under the linear-quadratic model, on the other hand, the effects of the two exposures are proportional to $D_1 + D_1^2/116$ and $D_1 + D_2^2/116$, respectively. The combined effect is proportional to the sum of these two numbers, and is less than the effect

of a single exposure to $D_1 + D_2$ rad, which is proportional to $(D_1 + D_2) + (D_1 + D_2)^2/116$. Thus for low-LET radiation there is a reduction in effect for fractionation and protraction of exposure, for all cancers except those of the thyroid gland and the female breast.

In practice, the reduction in effect due to fractionation of exposure in the above example is slight unless the sum of D_1 and D_2 is greater than 5 rad or so. (If $D_1 + D_2$ is less than 5 rad, then $(D_1 + D_2) + (D_1 + D_2)^2/116$ exceeds $D_1 + D_1^2/116 + D_2 + D_2^2/116$ by 2% or less.) Accordingly, for cancer sites for which the linear-quadratic model is appropriate, the Working Group suggests the following approach for calculating PCs for low-LET exposures separated in time or protracted over time: Generally, exposures occurring within a few months of each other can be combined (i.e., treated as a single exposure, with dose equal to the sum of the separate doses), provided that the sum of their doses is less than 5 rad. Consecutive acute exposures should not be combined if the total combined dose is greater than 5 rad. For protracted exposures, accumulations of 5 rad or less need not be subdivided unless the exposure extended over more than one year. Independence of effect cannot be assumed for exposures separated by less than 24 hours or so. In the absence of a detailed and reliable model, the Working Group recommends that cumulative exposures of 5 rad or more within a period of 24 hours or less be treated as if from a single acute exposure. This rule may result in the overestimation of the effects of exposures separated by a few hours. For very low dose rates the above approach gives results that are virtually the same (within 4%) as would be obtained if the quadratic (dose-squared) term were ignored. For a detailed example, see Chapter IX, Example 5. Also, see site-specific examples in Chapter X.

C. Time after Exposure

Clearly, time is required for a single transformed cell to develop into a clinically detectable cancer, and for that reason alone, a cancer detected within a few weeks or months after a particular radiation exposure would not be considered a possible consequence of that exposure. More generally, assumptions about the distribution of excess risk over time following exposure can strongly influence the PC calculations. There are two issues: how long does it take before there is a non-negligible excess risk, and how does the risk vary over time subsequently?

The BEIR III Committee used a plateau model for leukemia and bone cancer and both a constant absolute risk projection model and a constant relative risk projection model for other cancers, in order to extend their estimates of average excess risk, obtained from follow-up periods of 30 years or so, to estimated lifetime cancer risks. The Working Group faced a much more difficult problem, for two reasons: First, a PC calculation pertains to a specific cancer diagnosis at a particular time following one or more exposures to radiation, and not to risk averaged over a lifetime. Second, the charge to the Working Group was to provide a single "best" estimate and not an array of more or less plausible ones. Thus it was necessary to use specific time-to-response models which could, however, depend upon cancer site and upon individual characteristics such as age at exposure, sex, and radiation dose. Fortunately, research subsequent to the 1980 BEIR report, made possible mainly by the increased duration

of follow-up on the Japanese A-bomb survivors and other irradiated groups (see Chapter III-H), helped the Working Group to arrive at a number of assumptions needed for its calculations.

The 1980 BEIR report, as well as the published analyses reviewed in Chapter III-H, suggested that time from an acute exposure until diagnosis for radiation-induced bone cancer and leukemia follows wave-like distributions like the lognormal. Accordingly, the Working Group conducted analyses of data on time to diagnosis from a German series of patients treated by radium-224 injections for ankylosing spondylitis, and who later developed bone cancer at a rate more than 250 times that expected from baseline population rates (10), and leukemia data from A-bomb survivors with high radiation doses (11), supplemented by leukemia data from a British series of patients treated with X radiation for ankylosing spondylitis (12). Lognormal time-response models were fitted to these data, for all exposure ages combined and as partitioned by age at exposure.

The bone cancer data were found to conform closely to a lognormal distribution for time to response, with minimum 1.52 years, and for which the mean and variance on the logarithmic scale, after subtraction of the minimum, were 2.12 and 0.48, respectively (Figure V-1). The minimum value was the least precise of the three estimated quantities; virtually the same fitted probability distribution was obtained when the BEIR III minimum of 2 years was assumed a priori. There was no evidence that the distribution of time to response depended on age at exposure or on radiation dose.

The leukemia data were less easy to work with, partly because the possibility that a given high-dose case was not radiogenic could not be ruled out with as much confidence as with the bone cancer data, but mainly because the cancer data for the A-bomb survivors for the first 5 years after exposure lacked suitable denominators (11). The BEIR III minimum of 2 years for the latent period was assumed. Based on the British ankylosing spondylitis data (12), it was estimated that the average annual excess leukemia rate during the period 2-5 years after exposure was about half that during the next five years. From published analyses of the A-bomb survivor data (3,13) it was determined that acute leukemia (AL) and chronic granulocytic leukemia (CGL) have different temporal distributions following exposure, and that for AL, but not CGL, time to diagnosis depends on age at exposure. (Very few of the leukemias in the series are of types other than AL or CGL.) According to the Working Group's analysis, the fitted lognormal distribution for CGL had mean 2.68 and variance 1.51 on the logarithmic scale of time in years minus the assumed 2-year minimum (Figure V-2), while that for AL required an adjustment for age at exposure. The estimated mean on the logarithmic scale was $1.61 + .015 A_1 + .0005 A_1^2$, where A_1 denotes age at exposure, and the variance was 0.65. For AL, therefore, the fitted distribution predicts that with increasing age at exposure, radiation-induced cases tend to occur longer after exposure and to be more widely dispersed in time (Figure V-3). For leukemia in general, excluding the chronic lymphocytic form that apparently is not caused by radiation, the Working Group used a mixture of the estimated time-to-response curves for CGL and AL, weighted by .32 and .68, respectively (Figure V-4).

For leukemia and bone cancer the temporal distributions of risk imply that the plausibility of a causal connection between a particular cancer and a prior radiation exposure may depend strongly upon the length of the intervening time interval. For example, according to the time-to-response model described above, a radiation-induced bone cancer is about 6 times more likely to be diagnosed 5 years after exposure than 20 years after exposure; therefore, all other things being equal, the plausibility of a causal connection between a diagnosed bone cancer and a prior radiation exposure is greater for a 5-year interval from exposure to diagnosis than for a 20-year interval.

For cancers other than leukemia and bone cancer, the estimated probability of causation is independent of time from radiation exposure until cancer diagnosis, if that time is greater than 10 years. This is a consequence of the constant relative risk model for time to response which the Working Group adopted on the basis of published studies discussed in Chapter III-H. Because these studies pertained mainly to breast and lung cancer, the Working Group carried out a comparable analysis of stomach cancer among high-dose A-bomb survivors, and obtained results similar to those obtained for breast cancer and lung cancer.

The constant relative risk model applies only after some initial period, which the BEIR III Committee fixed at 10 years. The Working Group felt that this value was consistent with epidemiological findings for persons exposed at ages at which baseline incidence was already high enough for an appreciable number of excess cancers to be expected under the model, and that for younger exposure ages the practical importance of the initial period was small because few cancers, radiation-induced or otherwise, would be expected until much later than 10 years after exposure. On the other hand, the radiation-related excess risk is zero at the time of exposure, and assumes its eventual full value relative to baseline incidence after about 10 years. The Working Group felt that not enough is known about tumor growth kinetics to justify a distributional model for the time required for a single transformed cell to develop into a clinically detectable tumor; what is known, however, suggests that the risk of radiation-induced cancer (other than bone cancer and leukemia) is negligible for the first 5 years after exposure (see Chapter III-H). A discontinuity is biologically unlikely, and the Working Group therefore decided upon a cubic function of time to provide a smooth transition from an assumed zero excess for the first 5 years after exposure to the eventual constant relative excess after 10 years (Figure V-5), to be applied on the basis of time in whole numbers of years. In the table below, Y represents the integer part of time in years from exposure until diagnosis (e.g., 11 years, 10 months corresponds to Y = 11) and T(Y) is the corresponding proportion of the eventual relative excess applying at time Y:

Y:	0-4	5	6	7	8	9	10+
T(Y):	0	.074	.259	.500	.741	.926	1.000

PC estimates are most reliable, of course, when they are based altogether on observational data. Unfortunately, there are no series that provide followup data beyond 40 years after exposure, and most of the available longterm data pertain to the interval from exposure to

30-35 years. Use of the constant relative risk model of time-response for most solid tumors makes the dependence on the present PC tables for estimates beyond this interval less hazardous than would be the case if the constant risk model were to have been used. This is because absolute risks within each age-at-exposure cohort of A-bomb survivors have continued to rise steadily, tracking baseline mortality, well beyond the 1974 cut-off that was the basis for many of the BEIR coefficients. The constant relative risks resulting from these observations have been published through 1978 (4) and are seen in preliminary drafts of the current analysis that extend through 1982. For leukemia and bone cancer, the wave-like functions fall so precipitously after attaining their respective peaks that the Working Group has extended the tables beyond the period of observation to 49 years.

D. Age at Exposure

A rule that appears to hold for all radiation-induced cancers as a group, and for many cancer sites individually, is that excess risk declines relative to baseline risk with increasing age at exposure. Also, however, because excess risk tends to increase over time proportionally with baseline risk and because available data are limited to the period 30 years or so after exposure, absolute measures of risk tend to increase with increasing age at exposure. For cancers of the lung, digestive tract, and urinary system, which comprise a large part of both the excess and baseline cancer risk in exposed populations, this increase appears to be smooth (2,4). For some cancer sites, like the liver, bone, and, until recently, the thyroid gland, there was insufficient evidence on which to base estimates of variation by exposure age, and the BEIR age-specific risk coefficients for these sites are flat. Three important sites, however, are exceptions to the general rule.

A recent study of thyroid cancer incidence among A-bomb survivors indicates strongly that absolute, as well as relative, measures of risk are markedly reduced for adult compared to childhood exposures (5). Breast cancer, however, for which the existence of a risk following exposure during the first decade of life was only recently established (14,15), shows an increase in absolute risk with increasing age at exposure over the first two decades of life, but a marked decrease thereafter (6,16,17). To the 1980 BEIR Committee, which relied mainly on Japanese A-bomb survivor data for exposures after the age of 40, it seemed possible that the apparent absence of an excess might reflect a hormonal influence due to ovarian irradiation, or perhaps a difference between Japanese and western populations (2). More recently, however, a large survey of breast cancer mortality among Canadian women given multiple chest fluoroscopies during treatment for tuberculosis revealed the same pattern of greatly reduced risk for exposure after age 40 (17). Accordingly, the Working Group computed new age-specific breast cancer risk estimates from the most recent A-bomb survivor data (6), relying on a study of Swedish women given therapeutic X radiation for benign breast disease (16) to provide a smooth downward transition in risk from age 40 down to 75, at which age a zero excess was assumed.

For leukemia, there is a high absolute excess risk for exposures during the first decade of life, with a much lower excess for exposure at ages 10-19, and a steady increase for exposures at older ages (4). The BEIR report estimates, which were based on A-bomb survivor incidence data (3), do not vary smoothly with age, in that the coefficient for exposure ages 20-34 is higher than those for ages 10-19 and 35-49. The difference is far from significant statistically, however, and a similar pattern is not seen in data based on the British spondylitis series (18). Accordingly, the Working Group replaced the BEIR coefficients for exposure age intervals 10-19, 20-34, 35-49, and 50+ by values corresponding to a quadratic function of age, fitted by least squares using weights based on the variances of the BEIR estimates. No adjustment was made to the BEIR coefficient for exposure ages 0-9, about which the spondylitis data are uninformative.

Epidemiological data linking fetal radiation exposure to increased cancer risk largely pertain to exposure from pelvimetry examinations shortly before birth. The 1980 BEIR report presented an estimate of this risk based on the results of the Oxford Survey (19), as 25 excess leukemia deaths and 28 excess deaths from other cancers per million persons per year per rad for the first 12 and 10 years of life, respectively. The Committee did not, however, explicitly include these estimates in its tabulated estimates of lifetime risk following acute and chronic exposures to radiation. Even after allowing for the difference in follow-up (5-26 years for the A-bomb survivors vs. 0-12 years for the Oxford Survey) in the light of the calculated lognormal time-to-diagnosis distribution for exposure at age 0 (Table X.1.H), and allowing, with Stewart (20), for the possibility that estimated radiation doses in the Oxford Survey may have been too small by a factor of 2, the above estimate for leukemia is three times as high as an extrapolated estimate based on the leukemia coefficients used for the present report (Table VI-1). Experimental studies, in fact, suggest that there is little or no cancer risk associated with exposure during the middle uterine period, and that exposure during the late uterine stage is comparable in effect to exposure during infancy and early childhood (21-24). Given the uncertainties that remain about the magnitude of radiogenic risk of leukemia and other childhood cancers following fetal irradiation (see Chapter III-G), the Working Group is unpersuaded that cancer risk depends strongly upon whether or not the exposed person was in utero or postnatal, and suggests that in-utero exposures be treated no differently than postnatal exposures at age 0.

REFERENCES – Chapter V

1. National Cancer Institute, "Surveillance, Epidemiology, and End Results. Incidence and Mortality Data: 1973-1977." NCI Monogr. 57, U.S. Government Printing Office, Washington, D.C., 1981.

2. Committee on the Biological Effects of Ionizing Radiation, "The Effects on Populations of Exposure to Low Levels of Ionizing Radiation 1980." National Academy Press, Washington, D.C., 1980.

3. Ichimaru, M., Ishimaru, T. and Belsky, J. L., Incidence of Leukemia in Atomic Bomb Survivors Belonging to a Fixed Cohort in Hiroshima and Nagasaki, 1950-71. J. Radiat. Res. 19: 262-282 (1978).

4. Kato, H. and Schull, W. J., Studies of the Mortality of A-Bomb Survivors. 7. Mortality, 1950-1978: Part 1. Cancer Mortality. Radiat. Res. 90: 395-432 (1982).

5. Ishimaru, T., et al., Incidence of Thyroid Cancer among Atomic Bomb Survivors and Controls, Hiroshima and Nagasaki, 1958-1979: Relationship to Radiation Dose Absorbed by Thyroid Gland. Unpublished manuscript dated September 20, 1983.

6. Tokunaga, M., Land, C. E., Yamamoto, T., Asano, M., Tokuoka, S., Ezaki, E. and Nishimori, I., Incidence of Female Breast Cancer Among Atomic Bomb Survivors, Hiroshima and Nagasaki, 1950-1980. RERF Technical Report (in press).

7. Land, C. E., Cancers of the Digestive Tract and Accessory Organs. In "Radiation Carcinogenesis" (A. C. Upton, R. E. Shore and R. E. Albert, Eds.), in press. Elsevier North-Holland, New York, 1984.

8. Brown, J. M., The Shape of the Dose-Response Curve for Radiation Carcinogenesis: Extrapolation to Low Doses. Radiat. Res. 71: 34-50 (1977).

9. Land, C. E., Estimating Cancer Risks from Low Doses of Ionizing Radiation. Science 209: 1197-1203 (1980).

10. Mays, C. W. and Spiess, H., Epidemiological Studies of German Patients with Ra-224. In "Epidemiology Applied to Health Physics" (Proceedings of the Sixteenth Midyear Topical Meetings, Health Physics Society, Albuquerque, NM. January 9-13, 1983), pp. 159-166. National Technical Information Service CONF-830101.

11. Ichimaru, M., Ishimaru, T., Mikami, M., Yamada, Y., and Ohkita, T. Incidence of Leukemia in a Fixed Cohort of Atomic Bomb Survivors and Controls, Hiroshima and Nagasaki, October 1950-December 1978. Technical Report 13-81, Hiroshima, Radiation Effects Research Foundation, 1981.

12. Court Brown, W. M. and Doll, R., Mortality from Cancer and other Causes after Radiotherapy for Ankylosing Spondylitis. Br. Med. J. 2: 1327-1332 (1965).

13. Land, C. E. and Norman, J. E., Latent Periods of Radiogenic Cancers Occurring among Japanese A-bomb Survivors. In: "Late Biological Effects of Ionizing Radiation", Vol. 1, pp. 29-47. International Atomic Energy Agency, Vienna, 1978.

14. Tokunaga, M., Land, C. E., Yamamoto, T., Asano, M., Tokuoka, S., Ezaki, H. and Mishimori, I., Breast Cancer in Japanese A-bomb Survivors. Lancet 2: 924 (1982).

15. Hildreth, M. G., Shore, R. E. and Hempelmann, L. H., Risk of Breast Cancer among Women Receiving Radiation Treatment in Infancy for Thymic Enlargement. Lancet 2: 273 (1983).

16. Baral, E., Larsson, L. and Mattsson, B., Breast Cancer Following Irradiation of the Breast. Cancer 40: 2905-2910 (1977).

17. Howe, G. R., The Epidemiology of Radiogenic Breast Cancer. In "Radiation Carcinogenesis: Epidemiology and Biological Significance" (J. D. Boice, Jr., and J. F. Fraumeni, Jr., Eds.), pp. 119-129. Raven Press, New York, 1984.

18. Darby, S. C., Nakashima, E. and Kato, H., Parallel Analysis of Cancer Mortality among Atomic Bomb Survivors and Patients with Ankylosing Spondylitis Given X-ray Therapy. RERF Technical Report 4-84, Hiroshima, Japan, Radiation Effects Research Foundation, in press.

19. Bithell, J. F. and Stewart, A. M., Prenatal Irradiation and Childhood Malignancy. A Review of British Data from the Oxford Survey. Br. J. Cancer 31: 271-287 (1975).

20. Stewart, A. M., Radiation Cancers and A-bomb Survivors. Lancet 2: 1203 (1971).

21. Sasaki, S., Kasuga, T., and Kawashima, N., Influence of Physical and Biological Factors on Radiation Carcinogenesis: Age-dependence of Susceptibility to Radiation Carcinogenesis. In "Final Report: Risks due to Low Level Radiation Exposure," Project Research in FY 1973-1982. National Institute of Radiological Sciences (NIRS-M-47), Anagawa, Chiba, Japan, 1983.

22. Sasaki, S., Tsutomu, K., Sato, F., and Kawashima, N., Late Effects of Fetal Mice Irradiated at Middle or Late Uterine Stage. Gann 69: 167-1977 (1978).

23. Sasaki, S. and Kasuga, T., Life Shortening and Carcinogenesis in Mice Irradiated Neonatally with X Rays. Radiat. Res. 88: 313-235 (1981).

24. Sasaki, S. and Kasuga, T., Life Shortening and Carcinogenesis in Mice Irradiated at the Perinatal Period with Gamma Rays. In "Life Span Radiation Effect Studies in Animals: What Can They Tell Us?" (Proceedings of the 22nd Hanford Life Sciences Symposium, Richland, WA, Sept. 27-29, 1983.) DOE Symposium Series, Technical Information Center U.S. Department of Energy (in press).

Table V-1. SEER Baseline Cancer Incidence Rates (Cases per 100,000 per Year), 1973-1980, by Sex, Cancer Site, and Age at Diagnosis

Cancer Site: Males

Age	CGL	AL	LEUK	BONE	SALIV	ESOPH	STOM	COLON	LIVER	PANCR	LUNG	BRST	URIN	THYR
0-4	.	6.9	7.0	.1	.02	0	0	0	.4	0	0	—	.	0
5-9	.	3.2	3.5	.3	.01	0	0	0	.1	0	0	—	.	—
10-14	.2	2.4	2.5	1.3	.05	0	0	0	.1	0	0	—	.1	.2
15-19	.4	2.5	2.7	1.5	.09	0	0	0	.1	0	0	—	.7	.
20-24	.6	1.8	2.2	.7	.28	0	.1	.2	.2	0	.6	—	.4	.9
25-29	.8	2.0	2.9	.7	.41	.1	.3	.2	.3	.1	1.6	—	.3	1.2
30-34	1.0	2.2	3.4	.5	.57	.6	.7	1.2	.9	.5	2.3	—	.8	3.7
35-39	1.2	2.4	3.4	.5	.57	1.8	2.1	2.4	1.3	1.2	8.5	—	3.0	3.5
40-44	1.9	2.4	4.6	.8	1.08	4.9	4.1	5.2	2.3	3.6	24.0	—	5.5	3.7
45-49	1.8	4.4	5.6	1.0	1.01	9.1	8.8	9.5	3.8	6.6	61.4	—	12.8	3.8
50-54	3.6	5.8	7.7	1.2	1.74	15.4	15.5	18.8	6.6	14.0	116.7	—	23.5	4.4
55-59	4.4	8.2	11.4	1.7	2.23	22.7	24.1	34.3	10.4	23.3	192.2	—	42.2	4.4
60-64	5.5	13.4	17.1	2.1	2.56	30.2	42.0	61.9	15.2	38.2	295.1	—	69.3	4.4
65-69	7.7	18.2	24.1	1.7	3.46	34.9	58.1	104.4	18.1	55.0	409.1	—	106.0	5.9
70-74	12.2	31.2	39.2	2.1	4.48	33.6	79.6	166.3	23.1	74.0	491.6	—	156.1	6.3
75-79	19.0	45.3	58.6	3.2	7.10	34.5	113.7	243.3	22.1	91.5	527.8	—	216.6	6.7
80-84	18.9	58.6	78.6	1.9	8.15	32.9	142.0	328.4	23.0	98.0	462.5	—	277.0	7.6
85-98	18.9	64.8	86.4	2.7	8.19	35.5	157.0	448.1	21.2	115.6	373.0	—	335.3	6.1

Cancer Site: Females

Age	CGL	AL	LEUK	BONE	SALIV	ESOPH	STOM	COLON	LIVER	PANCR	LUNG	BRST	URIN	THYR
0-4	0	5.7	5.7	.1	.03	0	0	0	.3	0	0	0	2.1	0
5-9	.	2.7	2.8	.6	.13	0	0	0	.1	0	0	0	.6	.2
10-14	.	1.7	1.8	1.2	.19	0	0	0	.1	0	0	.	.2	.4
15-19	.2	1.4	1.4	.6	.25	0	.1	.2	.1	0	.2	.2	.6	2.2
20-24	.4	1.5	1.6	.4	.36	0	.2	.6	.2	.1	.6	.6	1.7	5.6
25-29	.6	1.5	2.1	.4	.58	.2	.4	1.2	.2	.3	1.8	8.6	2.7	9.0
30-34	.6	1.9	2.7	.2	.84	.7	1.0	2.3	.5	.8	5.8	27.2	5.3	9.7
35-39	1.0	2.3	3.4	.3	.88	1.8	2.8	5.1	.7	1.8	15.7	57.8	9.0	10.2
40-44	.9	3.6	4.5	.5	1.08	3.3	4.1	10.3	.8	4.8	31.9	106.3	14.2	9.3
45-49	1.5	4.6	5.4	.8	1.44	3.8	6.2	20.5	2.5	8.8	51.4	166.2	22.9	7.7
50-54	1.8	6.4	7.4	1.0	1.35	7.5	11.0	34.2	3.4	16.2	77.1	192.6	35.4	7.9
55-59	2.4	8.3	10.7	1.3	1.61	9.0	15.3	58.2	4.5	24.1	99.6	224.6	49.5	8.3
60-64	3.5	11.1	14.6	1.7	2.68	9.5	24.7	88.8	7.0	36.5	112.8	259.7	60.4	8.9
65-69	3.9	16.4	20.1	1.7	2.91	8.5	34.1	133.7	8.5	46.5	100.7	290.6	75.8	9.5
70-74	5.9	22.6	28.6	1.6	3.52	10.5	52.7	193.5	10.0	61.6	100.3	312.5	89.1	8.3
75-79	8.7	32.6	41.9	1.6	3.44	10.5	68.7	266.4	11.6	70.0	81.0	344.5	89.1	8.6
80-84	11.0	35.4	47.0	3.0	4.04	13.9	89.3	313.1	11.6	79.0	77.7	349.7	100.3	8.6
85-98	11.0	35.4	47.0	3.0	4.04	13.9	89.3	347.8	11.6	79.0	77.7	376.2	100.3	8.6

TABLE V-2. Individual Types of Cancer for Which the BEIR III
Report Provides Incidence Risk Coefficients and Those for Which the
Working Group Has Calculated the Probability of Causation

BEIR III	Working Group

Leukemia (all except CLL) + bone cancer	Leukemia, all except CLL
	  acute forms
	  chronic granulocytic

Bone	Bone and joint*
Thyroid	Thyroid
Breast	Breast
Lung	Lung
Esophagus	Esophagus
Stomach	Stomach
Intestine (colon)	Colon
Liver	Liver
Pancreas	Pancreas
Urinary organs	Kidney and urinary bladder
Lymphoma	
	Salivary gland

*Alpha radiation from radium-224 only.
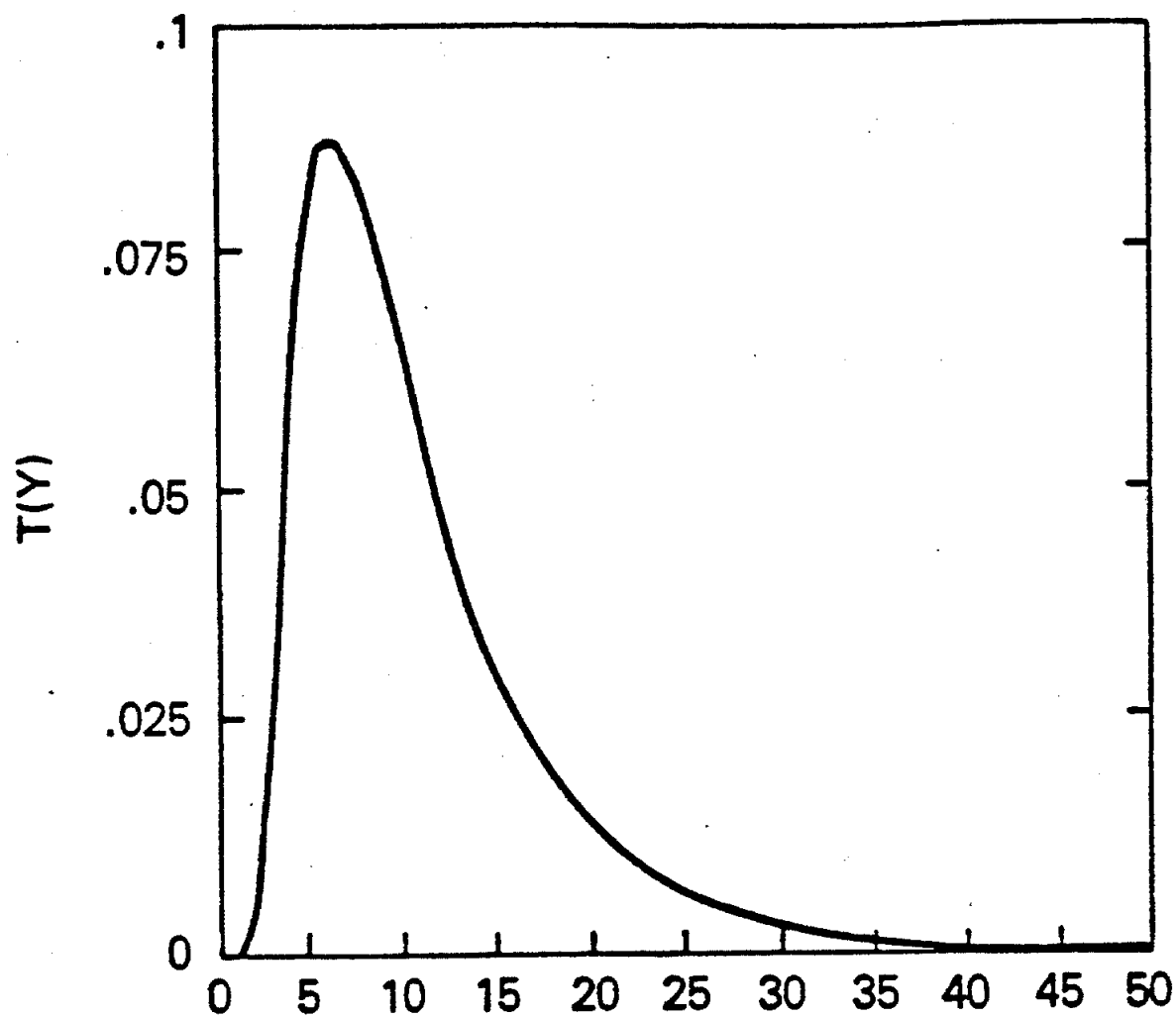
Figure V-1. Fitted time-to-tumor model for bone sarcoma induced by a brief exposure to radium-224. T(Y) is the probability of diagnosis within one year after time Y. (Data from reference 10.)
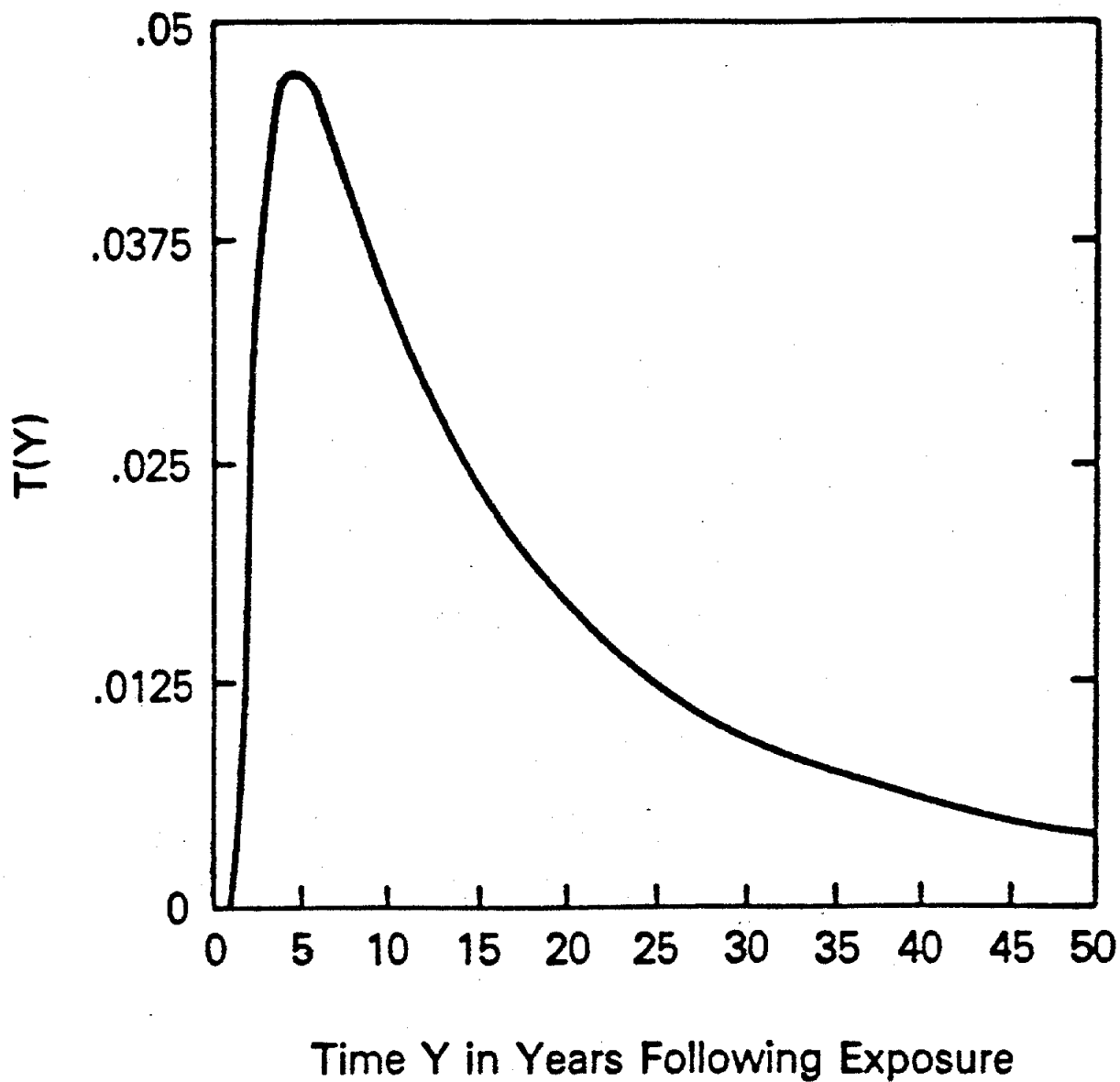
Figure V-2. Fitted time-to-tumor model for chronic granuloctyic leukemia induced by a brief exposure to ionizing radiation. T(Y) is the probability of diagnosis within one year after time Y. (Data from refs. 11 and 12.)
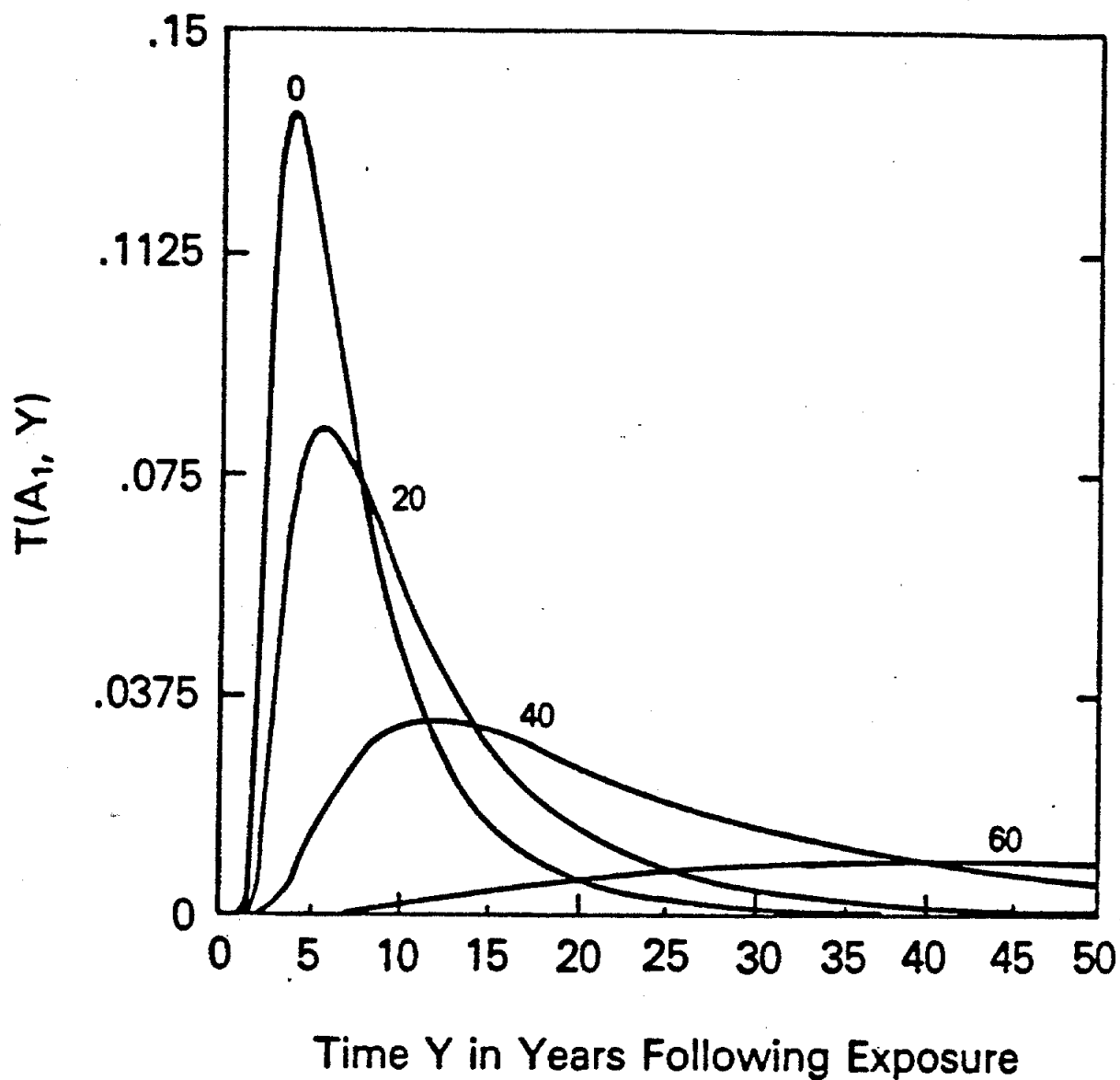
Figure V-3. Fitted time-to-tumor model for acute leukemia induced by a brief exposure to ionizing radiation at age A_1. $T(A_1,Y)$ is the probability of diagnosis within one year after time Y. Numbers within the graph indicate age at exposure. (Data from refs. 11 and 12.)
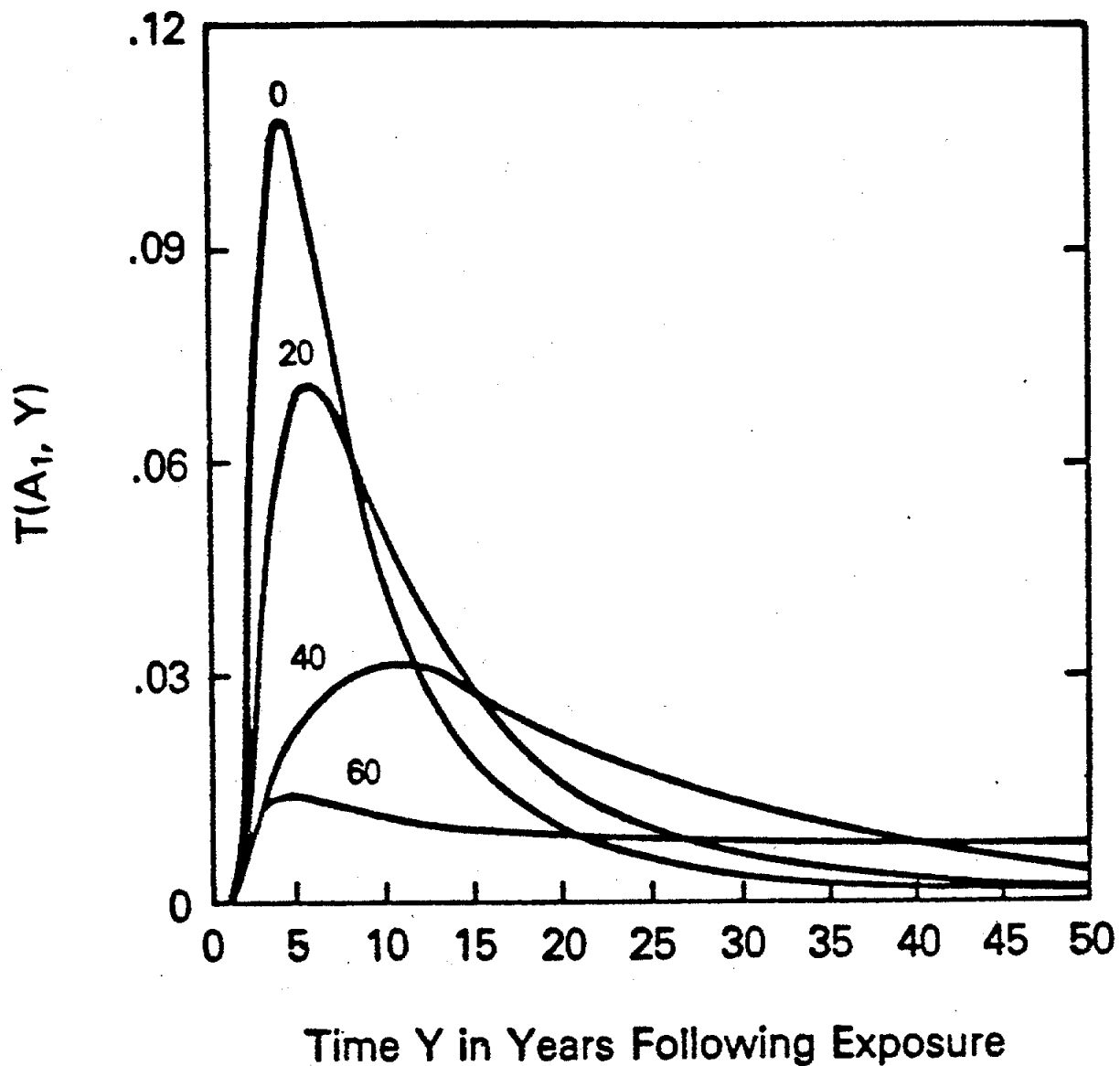
Figure V-4. Time-to-tumor model for leukemia (all types except chronic lymphocytic leukemia) induced by a brief exposure to ionizing radiation at age A_1. $T(A_1,Y)$ is the probability of diagnosis within one year after time Y. Numbers within the graph indicate age at exposure. (Data from refs. 11 and 12.)
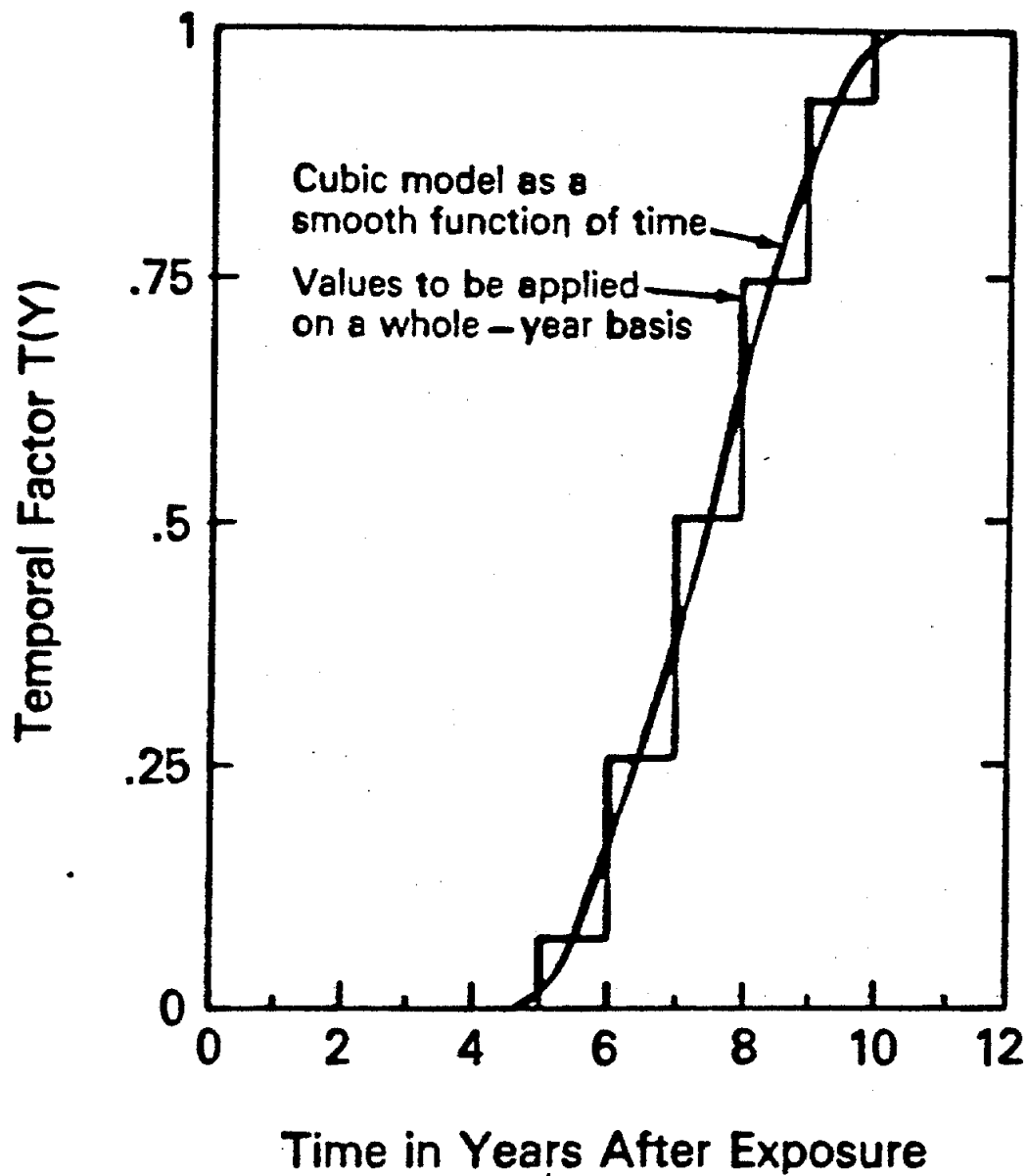
Figure V-5. Temporal factor T(Y) to be applied to
relative excess risk for cancers other than leukemia
or bone sarcoma.

CHAPTER VI: METHOD FOR ESTIMATING RELATIVE EXCESS RISK

AND CALCULATION OF PROBABILITY OF CAUSATION

A.   Coefficients of Absolute Excess Risk

The model assumed here for breast and thyroid cancer, for low-LET radiation, is that of risk as a linear function of organ dose, without threshold. For all other cancers considered, the linear-quadratic model is used for low-LET radiation (see Chapter V-B).

Table VI-1-A shows linear and linear-quadratic model risk coefficients for the incidence of excess cancers for specified periods after radiation exposure, by site, sex, and age at exposure, and for low-LET exposure, as adapted from the 1980 BEIR Report or from more recent data (see Chapter V, sections, A, B, and D). The tabulated coefficients represent the average absolute excess risks per 100,000 per year per unit increment in D or $D + D^2/116$, depending upon the dose-response model, where D is given in rad, over the specified follow-up periods for persons in the given ranges of age at exposure. Type-specific coefficients for acute and chronic granulocytic leukemia were derived from coefficients for leukemia of all types as follows: From A-bomb survivor data (1) it was determined that acute leukemias (AL) accounted for 68% of the excess leukemia risk due to radiation and chronic granulocytic leukemia (CGL) for the remaining 32%. Because this proportion did not appear to vary by age, the tabulated coefficients for leukemia were distributed accordingly. Tables VI-1-B and VI-1-C are for high-LET radiation and are only applicable to cancers of bone and joint and to lung cancer associated with exposure to radon.

PC calculations pertain to situations in which exposure age may be given for a single year of age, rather than an interval of 10 or more years, and smoothness of transition from one year of age to another is a desirable property of any calculational method that might be devised. Although the variation by age at exposure of the coefficients in Table VI-1 and in the BEIR report surely has a large random component, the Working Group did not, except in the cases of leukemia (see Chapter V-D) and lung cancer (see Chapter X-9), feel justified in smoothing this variation by assuming a parametric model for risk as a function of exposure age.

Accordingly, the tabulated coefficients were made specific to single years of age at exposure by an interpolation procedure. Each tabulated value was treated as if it pertained to the mean age of the corresponding interval, weighted by the expected length of follow-up, assuming a lifetable distribution (2) (see Table VI-2) of ages at exposure within the interval. Coefficients for single years of age were obtained by a cubic spline interpolation algorithm (3). For ages outside the range of interpolation (e.g., less than 5 for breast cancer or less than 25 for colon cancer, and greater than 58 for most sites), for which interpolation methods are notoriously unreliable, the following methods were used to minimize the effects of minor variations in the tabulated coefficients: BEIR coefficients for ages 0-9 or 10-19 deemed by the Working Group to have insufficient evidential basis for PC calculations were used as interpolation points to extend risk estimates to age 10 (stomach) or 20 (esophagus, colon, and

others). For lung cancer, the trend was linear over all ages (see Chapter X-9). For breast and thyroid cancers the trend in Table VI-1 from 10-19 to 0-9 was extended linearly to age 0, while for leukemia the interpolation routine produced an approximately linear extension which appeared to require no correction. For extrapolation to older ages an interpolation endpoint of zero risk at age 75 was used for breast cancer (see Chapter V-D), but for other sites the interpolation algorithm continued a smooth trend with increasing age at exposure which seemed to require no correction in view of the extremely limited information available on cancer risk from radiation exposures at age 60 or older.

B. Derivation of Coefficients for Calculating Relative Excess Risk

The interpolated absolute risk coefficients $e(A,S)$, where A denotes age at exposure and S denotes sex, were used to calculate coefficients from which the relative excess pertaining to a given year after exposure could be computed. For any given cancer site, age at exposure, and sex, let $P(Y)$ denote the absolute excess risk coefficient for Y years after exposure. The coefficient e was based upon observed cancer risk over a period of years after exposure, $y_1 \leq Y \leq y_2$ (see Table VI-1). The observed population was subject to attrition, mainly from the usual age-dependent force of mortality. Therefore, to an acceptable level of approximation, e is defined as the lifetable average of $P(Y)$ over the period $y_1 \leq Y \leq y_2$. Depending upon the way in which $P(Y)$ varies with time and with the age-specific baseline rate, the needed coefficients can be defined in terms of e. Two algorithms were used, one for leukemia and bone cancer, and the second for all other cancers.

1. Leukemia and bone cancer

For leukemia (AL and CGL) and bone cancer following brief irradiation type-specific lognormal distributions were obtained by fitting to data, and made specific to each age at exposure (see Chapter V-C). The distribution for all types of leukemia, from which chronic lymphocytic leukemia (CLL) was specifically excluded, was defined as a mixture of the distributions for AL and CGL, weighted by .68 and .32, respectively. The distribution, denoted by $T(A_1,Y)$ or $T(Y)$, depended upon age at exposure (A_1) for AL and therefore also for all leukemia except CLL, considered as a group, but T did not depend upon A_1 for CGL or bone cancer.

For each cancer type, for given (A_1,S), the time-specific coefficient $P(Y)$ can be written as

$$P(Y) = E \times T(Y),$$

where $E = E(A_1,S)$ denotes the probability that a radiation-induced cancer will be observed at some time after exposure, provided that no other cause of death intervenes. Therefore the coefficient e, which is the lifetable average of P over $y_1 \leq Y \leq y_2$, can be written as the product E, times the lifetable average of T. Solving for E, we obtain

$$E = e \times [L(y_1)+\ldots+L(y_2)]/[T(y_1)L(y_1)+\ldots+T(y_2)L(y_2)].$$

In the above formulation, L(y) denotes the lifetable value for the expected number of person-years at age $A_1 + y$ (the average of the lifetable probabilities of reaching ages $A_1 + y$ and $A_1 + y + 1$), using the 1970 U.S. lifetables (2) (see Table VI-2). The relative excess at age A_2, Y years after an exposure at age A_1, is given by

$$R(A_1,A_2,Y,S) = F \times T(A_1,Y) \times E(A_1,S)/I(A_2,S),$$

where F denotes an appropriate function of dose. $I(A_2,S)$ denotes the baseline incidence of cancer of the given site and type for a person of age A and sex S, as determined from the SEER values in Table VI-3 by an interpolation process analogous to that used to obtain the values $e(A_1,S)$. In the above formulation Y assumes only integer values, being the integer part of the time in years from exposure to diagnosis (e.g. if that time is 12 years and 11 months, Y = 12).

Although the 1980 BEIR Committee presented risk coefficients for bone sarcoma resulting from exposure to low-LET radiation, these coefficients were derived by the use of conventional quality factors from coefficients appropriate for exposure to alpha radiation (4, pp. 411-418). Bone sarcomas were seen above 67 rad alpha dose to the endostial layer, which corresponds, using a constant quality factor of 20, to 1300+ rem dose equivalent. Bone sarcoma has not been observed in excess among the Japanese atomic bomb survivors (4, p. 416), and in patients treated by X radiation for ankylosing spondylitis cases have been seen only in association with bone doses well above 1000 rad (4, p. 413). The Working Group, while convinced of the validity of the BEIR estimate for bone sarcoma following brief irradiation from radium 224, did not feel that there was a sufficient basis for extending it to low-LET radiation at doses below 1000 rad or to other forms of high-LET radiation. Accordingly, estimates for bone cancer are presented only for high-LET radiation, from radium-224 (see Table VI-1-B).

2. <u>Cancers other than leukemia and bone cancer, following exposures to low-LET radiation</u>

For other cancers, the temporal distribution of excess risk over time after exposure was assumed to be proportional to the variation of baseline incidence by age, at least beyond 10 years after exposure. In other words, for given (A_1,S), the ratio

$$K = P(Y)/I(A_2,S),$$

where (roughly) $A_2 = A_1 + Y$, was assumed to be constant for Y > 10. It was enough, therefore, to calculate, and tabulate, this ratio. Because the absolute risk coefficient $e = e(A_1,S)$ is the lifetable average of P(Y) over the follow-up period $y_1 \leq Y \leq y_2$ given in Table VI-1, it can also be expressed as the lifetable average over that period of K x I'(Y), where $I'(Y) = I(A_2,S)$ for $A_2 = A_1 + Y$. Because K does not depend upon Y for Y > 10, the relationship can be inverted to solve for $K = K(A_1,S)$:

$$K = e \times [L(y_1)+...+L(y_2)]/[I'(y_1)L(y_1)+...+I'(y_2)L(y_2)].$$

For $Y > 10$ years, the relative excess risk is simply $K(A_1,S)$ multiplied by an appropriate function F of radiation dose. There was, therefore, no requirement to tabulate the temporal distribution of risk or the baseline risk, as was done for leukemia and bone cancer. But because the relative excess must begin at zero and reach its full value after 10 years, and because biological considerations demand a smooth transition (see Chapter III-H), we have represented this transition by T, as given below and in Chapter V-C, in the case of cancers other than leukemia or bone cancer.

Y:	0-4	5	6	7	8	9	10+
T(Y):	0	.074	.259	.500	.741	.926	1.000

As before, Y denotes the integer part of time in years from exposure until cancer diagnosis. Thus, the relative excess Y years following radiation exposure at age A_1, for a person of sex S, is

$$R(A_1,Y,S) = F \times T(Y) \times K(A_1,S).$$

3. The special case of lung cancer following exposure to inhaled radon daughters

The 1980 BEIR report (4) gave a single set of linear-model coefficients to be applied to low-LET radiation and, with a suitable Q factor, to high-LET radiation from inhaled radon daughter products. The Working Group found the BEIR coefficients to be difficult to use, as discussed in Chapter X-9, and calculated separate absolute risk coefficients for exposures from external, low-LET radiation based on A-bomb survivor data. For inhaled radon daughter products, the Working Group adopted relative risk coefficients based on a review by Jacobi (5) of data from various studies of uranium miner populations. These estimates, as discussed in Chapter X-9, pertain to cumulative exposure in Working Level Months (WLM), and express excess risk as a percentage of underlying risk per WLM. The estimates do not depend upon sex or age at exposure, but take account of a possible difference in the method of measuring radon levels in U.S. mines before about 1961 as compared to after that time and in other countries (Table VI-1-C).

REFERENCES - Chapter VI

1. Ichimaru, M., Ishimaru, T., and Belsky, J. L., Incidence of Leukemia
   in Atomic Bomb Survivors Belonging to a Fixed Cohort in Hiroshima and
   Nagasaki, 1950-71. J. Radiat. Res. 19: 262-282 (1978).

2. "U.S. Decennial Life Tables for 1969-71," Vol. 1, No. 1, DHEW
   Publication No. (HRA) 75-1150, U.S. Department of Health,
   Education, and Welfare, Public Health Service, Health Resources
   Administration, National Center for Health Statistics, Rockville,
   Maryland (May 1975).

3. Akima, H., A New Method of Interpolation and Smooth Curve Fitting
   Based on Local Procedures. J. Assoc. Comput. Mach. 17: 589-602
   (1970).

4. Committee on the Biological Effects of Ionizing Radiation, "The
   Effects on Populations of Exposure to Low Levels of Ionizing
   Radiation: 1980." National Academy Press, Washington, D.C., 1980.

5. Jacobi, W., Paretzke, H. G., and Schindel, F., Lung Cancer Risk
   Assessment of Radon-Exposed Miners on the Basis of a Proportional
   Hazards Model. In "Proceedings of the International Conference
   on Occupational Radiation Safety in Mining", Oct. 14-18, 1984,
   Toronto, Canada, in press.

Table VI-1-A. Absolute Risk Coefficients: Absolute Excess Cancer Incidence per 100,000 Persons per Year per Rad (Organ Dose) at Low Levels of Low-LET Radiation, by Site, Sex, and and Exposure Age, Averaged over the Specified Follow-up Period

Site	Exposure Age	Years[1] Follow-up	Dose-response Model	Sex M	Sex F
Leukemia[2] (all types except CLL)	0-9	5-26	Linear-Quadratic	.173	.110
	10-19	5-26		.0854	.0543
	20-34	5-26		.0846	.0538
	35-49	5-26		.105	.0670
	50+	5-26		.156	.0990
Salivary[2]	0-14	10-30	Linear-Quadratic	.00104	.00104
Esophagus[3]	20-34	10-30	Linear-Quadratic	.0052	.0052
	35-39	10-30		.0084	.0084
	50+	10-30		.0224	.0224
Stomach[3]	10-19	10-30	Linear-Quadratic	.0160	.0160
	20-34	10-30		.0308	.0308
	35-49	10-30		.0508	.0508
	50+	10-30		.134	.134
Colon[3]	20-34	10-30	Linear-Quadratic	.0208	.0208
	35-49	10-30		.0336	.0336
	50+	10-30		.0892	.0892
Liver[3]	20-34	10-30	Linear-Quadratic	.028	.028
	35-49	10-30		.028	.028
	50+	10-30		.028	.028
Pancreas[3]	20-34	10-30	Linear-Quadratic	.018	.018
	35-49	10-30		.030	.030
	50+	10-30		.0788	.0788
Lung[2]	10-19	10-33	Linear-Quadratic	.030	.030
	20-34	10-33		.056	.056
	35-49	10-33		.086	.086
	50+	10-33		.120	.120
Breast[2]	0-9	10-35	Linear	—	.38
	10-19	10-35		—	.76
	20-29	10-35		—	.49
	30-39	10-35		—	.49
	40-49	10-35		—	.13
	50+	10-35		—	.08
Urinary[3]	20-34	10-30	Linear-Quadratic	.0200	.0200
	35-49	10-30		.0368	.0368
	50+	10-30		.0648	.0648
Thyroid[2]	0-9	10-34	Linear	.15	.50
	10-19	10-34		.15	.50
	20-34	10-34		.05	.15
	35-49	10-34		.05	.15
	50+	10-34		.05	.15

Table VI-1-B. Linear-model BEIR Absolute Risk Coefficients by Sex for
Bone and Joint Cancer Following Exposure to Alpha Particle Radiation
from Injected Radium-224: Absolute Excess Incidence per 100,000
Persons per Year per Rad to the Endosteal Layer

Exposure Age	Years Follow-up[1]	Sex	
		M	F
All	0-30	.10	.10

Table VI-1-C. Linear-Model Relative Risk Coefficient R for Lung
Cancer Following Exposure to Alpha Particle Radiation from Inhaled
Radon Daughters: Percent Excess Incidence per Working
Level Month, by Source of Data (Reference 5)

Exposure Age	Source of Data	Estimate (R)
All	Combined Uranium Miner Data	1.2
All	U.S. Miners, Exposed Before 1961	0.7
All	U.S. Miners, Exposed 1961 or Later	1.5

[1]Observed years of expression over which excess risk was averaged to
produce the risk coefficients shown. PC estimates for events beyond the
intervals shown lack a direct observational basis.

[2]Coefficients derived by Working Group; see Chapter X for details.

[3]Coefficients derived from BEIR (reference 4, p. 198, Table V-14).
Conversion of the linear-model BEIR coefficients to linear coefficients
in a linear-quadratic model involved dividing them by 2.5. Note that the
original BEIR coefficients were given per 10^6 person-year-rad.

TABLE VI-2 – U S 1970 LIFETABLE, BY SEX AND AGE, ALL RACES COMBINED [1]

Age	Sex Male	Female	Age	Sex Male	Female	Age	Sex Male	Female
0	1.000000	1.000000	37	.9261400	.9574150	74	.4295750	.6473600
1	.9887750	.9912700	38	.9233600	.9557600	75	.4019100	.6234450
2	.9769000	.9819650	39	.9203600	.9539600	76	.3738800	.5978550
3	.9757900	.9810150	40	.9171050	.9519950	77	.3456600	.5706400
4	.9749550	.9803450	41	.9135750	.9498650	78	.3175000	.5419050
5	.9742650	.9798000	42	.9097000	.9475650	79	.2897100	.5117750
6	.9736700	.9793400	43	.9056300	.9450800	80	.2625800	.4804150
7	.9731250	.9789450	44	.9011400	.9423850	81	.2362950	.4479700
8	.9726100	.9785900	45	.8962450	.9394550	82	.2109550	.4145900
9	.9721350	.9782700	46	.8909050	.9362700	83	.1866850	.3805650
10	.9717100	.9779800	47	.8850950	.9328100	84	.1636800	.3463250
11	.9713400	.9777150	48	.8787900	.9290750	85	.1421000	.3122950
12	.9710000	.9774650	49	.8719550	.9250650	86	.1219800	.2787200
13	.9706300	.9772050	50	.8645500	.9207550	87	.1033100	.2457300
14	.9701450	.9769150	51	.8565350	.9161200	88	.0861900	.2137050
15	.9694500	.9765600	52	.8478550	.9111350	89	.0708100	.1832950
16	.9684900	.9761200	53	.8384450	.9057750	90	.0573250	.1550900
17	.9672550	.9755950	54	.8282350	.9000200	91	.0457500	.1293750
18	.9657600	.9749900	55	.8171550	.8938500	92	.0359550	.1061900
19	.9640600	.9743350	56	.8051700	.8872400	93	.0277800	.0855900
20	.9622150	.9736550	57	.7922550	.8801550	94	.0210700	.0676900
21	.9602450	.9729600	58	.7783850	.8725700	95	.0156600	.0525400
22	.9581450	.9722550	59	.7635500	.8644750	96	.0114050	.0400400
23	.9559350	.9715350	60	.7477350	.8558450	97	.0081600	.0299800
24	.9536850	.9707950	61	.7309300	.8466500	98	.0057500	.0220850
25	.9514800	.9700400	62	.7131350	.8368600	99	.0039950	.0160300
26	.9493700	.9692700	63	.6943500	.8264100	100	.0027400	.0114800
27	.9473600	.9684750	64	.6745800	.8152200	101	.0018550	.0081150
28	.9454400	.9676550	65	.6538150	.8032050	102	.0012400	.0056650
29	.9435650	.9668000	66	.6320450	.7902900	103	.0008200	.0039100
30	.9416750	.9659000	67	.6092800	.7764350	104	.0005350	.0026700
31	.9397300	.9649450	68	.5855700	.7615500	105	.0003450	.0018050
32	.9377150	.9639200	69	.5610150	.7455700	106	.0002200	.0012100
33	.9356250	.9628150	70	.5357500	.7284250	107	.0001400	.0008098
34	.9334450	.9616250	71	.5099050	.7100800	108	.0000900	.0005380
35	.9311450	.9603350	72	.4835750	.6905250	109	.0000550	.0003380
36	.9287250	.9589350	73	.4568000	.6696700	110	.0000200	.0001370

Chapter VII: SOURCES OF UNCERTAINTY

A. Introduction

P.L 97-414 requires that the tables on probability of causation "shall be devised from the best available data that are most applicable to the United States, and shall be devised in accordance with the best available scientific procedures and expertise."

The statement by the President, on the occasion of his signing the Orphan Drug Act, expresses the Administration's reservations in regard to the preparation of the tables:

> "...there is as yet no consensus among radiation experts in relating human cancers and exposure to low levels of radiation. Yet, Section 7 mandates that probability of causation tables be calculated for even very small dose levels. Accordingly, I am directing the Secretary of Health and Human Services to complete the tables to the extent that may be possible and scientifically responsible, in light of the analysis also mandated by Section 7, which requires him to 'assess the credibility, validity, and degree of uncertainty associated with such tables.'"

What follows is a discussion of the many sources of uncertainty that should be recognized in connection with the use of the tables.

The probability-of-causation (PC) tables bring to bear on the adjudication of claims the very extensive information available on the risk of radiogenic cancer. Although we know more about the effects of ionizing radiation than any other carcinogen, and much of the knowledge is quantitative in form, our present knowledge is far from complete, and the tables can be regarded as no more than a guide to causation in the particular case. However, even an imperfect guide that summarizes the relevant literature in such a way that it can be brought to bear on the individual case should be helpful in determining whether a prior exposure to radiation was a significant factor.

Each element of the PC calculation has its own uncertainties, some of which are interdependent: choice of sites and cell-types for which tables can be prepared, baseline incidence, absorbed radiation dose, dose rate, minimum latent period, time to tumor recognition, choice of dose-response function, radiation risk coefficient, choice of time-response function, and the influence of individual host factors and competing etiologic influences. In Section VII-O an effort has been made to integrate most of these sources of uncertainties into an overall assessment of the accuracy that can be ascribed to any value of PC.

B. Sites of Cancer and Cell-Types

Although ionizing radiation has been shown to produce a very wide array of human cancers, for certain cell-types, e.g., chronic lymphocytic leukemia, radiation seems not to be detectably carcinogenic. For many

sites and cell-types, the empirical evidence is simply inadequate to establish or deny carcinogenicity, and for some, e.g., multiple myeloma, the evidence seems rather controversial (see Chapter X, Section 13). Authoritative lists of cancers considered to be radiogenic (1-4) are based on judgment as to the sufficiency of the human data available and the cogency of the evidence involving radiation as a cause. As a practical matter, however, even if a particular tissue is considered to be sensitive to the carcinogenic force of ionizing radiation, useful PC tables cannot be calculated in the absence of reasonably good estimates of risk coefficients. It is this requirement, for example, that limits the preparation of tables by cell-type to the leukemias. There are recent reports, for example, linking brain cancer with exposure to ionizing radiation (5,6) but none provides the kind of information that would be required for PC calculations. Further, as has been noted for the various types of leukemia, it remains possible that differentials may ultimately be established for the risks of certain cell-types among the solid tumors. If there are large probabilities of causation that involve sites of cancer other than those selected for the PC tables, those cancer sites must be quite rare.

The Working Group accepted the BEIR III list of radiogenic cancers with the following modifications: (a) lymphomas (including multiple myeloma) were deleted; (b) salivary gland cancers were added; and (c) "other" sites, needed by the BEIR III Committee in order to estimate the totality of radiogenic cancer, and for which no real data exist, were excluded. Of these changes, the first is discussed in Chapter X, Sec. 13, the second in Chapter X, Sec. 3. Sites of cancer for which PC estimates can be made, but for which the quantitative data are least reliable, are salivary glands, esophagus, pancreas, liver, urinary bladder and kidney.

C. Source Tables of Cancer Incidence in the U.S. Population

Age- and sex-specific SEER rates for the U.S.A are averages for the period 1973-1981 and for 10 areas containing about 10 percent of the U.S population. Although the SEER sample is not a probability sample, it is reasonably representative of the U.S population as judged by mortality rates. The quality of the data is very high, only 1.4 percent of reported cases depending on death certificates alone, and 92 percent being microscopically confirmed (7). Geographic and ethnic variations are very real, of course, especially for certain anatomical sites (7). In addition, over the period of interest there have been important changes in the incidence of cancer for certain sites, especially stomach and lung (7-9). Although incidence data are not available systematically over time in the U.S., there are bench-mark data for 1947 and 1969-1971, and for some sites, especially lung and stomach, mortality data adequately reflect incidence. Incidence and mortality from stomach cancer have been moving down steadily for some time. For example, the death rate for white males that was 16 per 100,000 per year in 1960 had fallen to 8.2 by 1977. Conversely, death rates for lung cancer have been increasing rapidly over this period, the comparable rates for white males being 38 in 1960 and 68 in 1977. Changes in rates for other sites are less dramatic or seem less certain at the level of incidence. For example, mortality from thyroid cancer has been falling but there are indications of a 10 percent increase in incidence from 1970 to the average for 1973-1981. There are also some changes for non-whites of

which the most significant is for the esophagus: the mortality rate for non-white males that was 10 in 1960 had risen to 14 by 1977.

Among the ten SEER regions, there is a fair amount of variability for some cancer sites (Table VII-1). For example, the incidence of lung cancer may vary by as much as a factor of three between the SEER regions with the lowest and highest rates. Table VII-2 exhibits for each kind of cancer the largest and smallest ratios for any area to the All Areas incidence rate. Although a few of the extreme ra s are based on small numbers of incident cases, and hence are subjec large sampling variability (e.g., the ratio of 0.26 for esophageal cer in females in Utah is based on only nine cases) most of the ratios are fairly stable with respect to sampling variability: the very high ratio of 2.14 for stomach cancer in Hawaii males is based upon 442 cases. Most of the variability exemplified in Table VII-2 must be considered real.

Explanations for some of the variation come readily to mind: Hawaii has a very diverse ethnic mix, and the high ratios for thyroid and stomach cancer, and the low ratio for breast cancer, result from that fact, as an examination of ethnicity-specific rates in Hawaii makes clear (7). The low ratios in Utah for cancers of the lung and bronchus, esophagus, and colon presumably result from the well-known differences in life style of the Mormon populations of that state. To the extent that the low ratios for lung and bronchus reflect a high proportion of non-smokers, that effect will be accounted for if smoking history is considered by the method explained in Chapters IV and IX.

D. Minimal Latent Period

Time to tumor recognition is approximated by the interval from exposure to date of diagnosis. This approximation may be subject to "error," in that diagnosis may be delayed beyond the time when it might have been made, but it would be unusual if the delay were more than a year or two, except in the case of thyroid cancer. Most incidence rates for cancer do not change rapidly over such short age intervals. An "error" of this kind could be significant only if it affected whether or where the interval from exposure to tumor detection fell within the period over which the minimum latent period is smoothed as described in Chapter V-C; e.g., 5.0-9.9 years for most solid tumors.

The minimum latent period assumed in the calculation of PC tables is empirically based, but can be only roughly estimated for solid tumors. The BEIR III report (1) gives a minimal latent period of 2-4 years between exposure and tumor detection for leukemia and bone cancer, and this range seems well established. The BEIR III value of 10 years given as the minimal latent period for solid tumors is very approximate, as it is not site-specific and all indications are that the interval varies greatly with age at exposure, being longer for younger than for older individuals. For younger individuals especially, the uncertainties are appreciable, but of little practical effect when the constant relative risk model of time-response is used.

Although the Working Group starts from the assumption of minimum

latent periods of two years for leukemia and bone (brief irradiation only) and 10 years for the other cancers, to avoid the sharp step-up from 0 to full effect at these points, it has "smoothed" the minimum latent period as described in Chapter V-C. For leukemia and bone cancer, for which a fitted "wave" function represents the distribution of excess cases over time, no such additional smoothing was necessary. For the other forms of cancer, however, the process of smoothing is rather arbitrary as empirical data are lacking. The interval 5.0-9.9 years after exposure may not be the optimal choice, and the cubic function used to graduate the effect of time to diagnosis within this interval may not be the best function to use.

For bone cancer and leukemia the minimal latent periods, 1.5 and 2 years, respectively, have a range of uncertainty from about 1 to 4 years. For the solid tumors the Working Group has assumed that the full expression of the increased relative risk occurs as early as ten years after exposure, and that the increased risk builds up in the interval 5 to 9 years after exposure. It is thought that these assumptions, in all probability, under-estimate the required period of latency. It is only with respect to intervals of 5-14 years between exposure and diagnosis that this source of uncertainty is meaningful.

E. Dose-Response Function

In general, it has not been possible to show that doses of a few rad have any influence on the likelihood of cancer since the risk, if any, is lost in the background of natural incidence. It should be noted that the BEIR committee was unwilling to make estimates for acute doses below 10 rad or for continuous exposure to less than 1 rad per year. Although it has been suggested that a dose as low as 2-3 rad during fetal life may be leukemogenic (10,11), these studies have been questioned by some because exposure generally occurred on a selective basis associated with the medical indications for X-ray pelvimetry. Comparable studies in which radiation exposure occurred on a non-selective basis from routine pelvimetry (12) or atomic bomb radiation (13) do not suggest that doses of 2-3 rad have any effect, but these series are small (see Chapter III-G).

In the very low dose region useful estimates cannot be made without interpolation between the risk at 0 rad and the demonstrable and measurable risk in the relatively high dose region, generally at or beyond 100 rad. In the absence of a satisfactory theory of radiation carcinogenesis to guide the choice of mathematical function with which to perform the interpolation, considerable uncertainty attaches to interpolated risk coefficients in the low-dose range. In the BEIR III report, for example, the calculated linear coefficients (i.e., the limiting slopes of the dose-response curves at very low doses) for the risk of leukemia from low-LET radiation are 0.99 ± 0.93 excess cases per 10^6 persons per year per rad under the so-called linear-quadratic model and 2.24 ± 0.60 under the linear model. In the "pure" quadratic model, of course, the linear term vanishes entirely. At 2 rad the risk of leukemia under these three models is 2.0 per million persons per year for the linear-quadratic, 4.5 for the linear, and 0.056 for the "pure" quadratic. Corresponding values for all forms of cancer, other than leukemia, considered as a group, are

2.8, 6.94, and 0.074. The linear model is generally considered to over-
estimate the risk in the low dose range, although it is possible to post-
ulate a distribution of susceptible individuals in the population such
that a power curve might better describe the dose-response relationship
(14). In this latter case, low-dose risk estimates might exceed those
based on the linear model, but the applicability of such estimates to the
calculation of PC values would be questionable.

Animal experiments in which a wide range of dose is employed often
show a turn-down in the dose-effect curve at high doses, an observation
attributed to cell-inactivation. The BEIR III committee did not employ a
model with a term that brings down the curve at high doses since it was
concerned with low dose estimation and, since the LD_{50} for acute whole-
body doses to man is in the range of 350-450 rad, the turn-down is not as
definite in the data on the A-bomb survivors. But for partial-body
irradiation this aspect of dose-response may have considerable importance
when organ doses are very high, as is suggested by the low incidence of
second cancers in patients treated with therapeutic doses of radium and X
radiation for cervical cancer. Failure or inability to correct for this
phenomenon has the effect of over-estimating the PC values at very high
doses.

As indicated in Chapter V-B, for exposure to low-LET radiation the
Working Group has chosen the linear-quadratic dose-response model for all
forms of cancer except cancers of the breast and thyroid. Since the co-
efficient of the linear term of the linear-quadratic dose-response function
was generally derived from the corresponding coefficient of the linear
function employed in the BEIR report for cancer incidence, and the procedure
was merely to divide the latter by 2.5 to create the coefficients used
here, this factor provides one measure of the uncertainty associated with
the choice of the dose-response function, at least in the range of 20 rad
or less. Above 20 rad the $D^2/116$ term becomes increasingly important;
the risk on the linear model would be less than 2.13 times that on the
linear-quadratic model, not 2.5. In addition, there is an uncertainty in
the factor 2.5 that rests on the choice of the cross-over dose, estimated
in Section VII-O below to range from about 1.0 to 6.3.

F. Influence of Age at Exposure

Although the BEIR III risk estimates (1) in Table VI-I here represen-
ted a consensus of informed scientific opinion at the time, there were
few human data to substantiate some of the risk estimates for exposures
below age 10 or, in some cases, below age 20. Although for a few cancers
(thyroid, breast, lung, leukemia) the Working Group has modified the BEIR
1980 risk values on the basis of later data not available to the BEIR
Committee, for most of the cancer types the BEIR risk estimates have been
adopted.

The accuracy of a risk estimate is limited by the number of cases of
a particular cancer observed among persons whose doses were at least 10
rad. Even when that number is reasonably large, the risk estimate may be
subject to considerable uncertainty but, when the number is small, the
uncertainty may be so large that the risk estimate is unusable for the

present purpose. The most recent mortality data concerning the Japanese A-bomb survivors that were available to the BEIR Committee apply to the period from five to thirty years following the radiation exposures (15).

Age 0-9 in 1945. For the digestive organs and peritoneum, there evidently were barely enough data to support an estimate of risk for the class as a whole; risk estimates for pancreas, liver, etc are supported by no data. For these cancers in children, no data were available to the BEIR Committee except those from the Japanese survivors. Table VII-4 provides no basis for calculating PC's for exposures at ages under 10 years for cancers of any of the digestive or respiratory organs. PC's cannot be calculated because the underlying BEIR risk coefficients are not supported by adequate data.

Age 10-19 in 1945. The data in Table VII-5 may be sturdy enough to support PC's for stomach cancer, but not for any other individual digestive organ. The number of deaths from respiratory cancer is also very small, but the coefficients in Table VI-1 were based on the later 1950-1978 report (10), with 15 deaths in this age group from lung cancer. The tables in Chapter X, therefore, provide the basis for calculating PC's for this age group at exposure only for the stomach among the digestive organs, as well as for lung cancer, bone cancer, leukemia, thyroid cancer, breast cancer, and cancer of the salivary gland.

The next BEIR report will be able to take advantage of extensive data compiled since the BEIR 1980 report (1) was prepared, including eight additional years of follow-up of the Japanese A-bomb survivors. Risk estimates for young persons, and knowledge of latent periods applicable to them, will be much improved, and future versions of these tables can then provide PC's for ages and cancer types for which presently available data are inadequate.

In addition to the extreme uncertainties that make it inadvisable to attempt estimates of risk at the younger ages, the statistical uncertainties in age-specific risk coefficients arising from sampling error, and the possibly atypical character of some of the populations whose experience has been drawn upon for epidemiologic studies, there is the technical problem of interpolation among the risk coefficients calculated for age intervals to produce estimates for single years of age, as well as the problem of extrapolation in the age range beyond the given data points. Knowledge of age at exposure as a determinant of risk is too limited to provide sure guidance for the choice of a fitting procedure for each site, and different methods naturally give somewhat different results, especially at the oldest ages. The BEIR coefficients are given in age-at-exposure intervals of 0-9, 10-19, 20-34, 35-49, and 50+. For some sites it makes a great deal of difference, particularly at ages 65 and older, how the fitting is performed. Linear interpolation between the midpoints of adjacent age intervals would produce a sequence of irregular changes with age and leave undefined the regions under age 5 and over age 65. A cubic spline interpolation provides a smoother sequence of values within the range bounded by the midpoints of the extreme age groups, e.g., 4.5 to 58 or 59 in the case of leukemia, and 24.5 to 58 or 59 in the case of colon cancer, but the behavior of the spline function outside this range can be difficult to predict. These problems have been

handled as described in Chapter V-D, by a method that seems reasonable and satisfactory to the Working Group. It must be admitted, however, that other plausible approaches might have yielded different estimates for very young and very old exposure ages.

G. Sex

Sex differences in the absolute risk of radiogenic cancer are apparently small (1), except for breast cancer, thyroid cancer, and leukemia, but the topic is not fully developed in the radiation literature. In the BEIR III report the age-specific absolute risk coefficients are identical for the two sexes, except for the 3 sites named, but when, as here, these coefficients are employed to derive relative risk factors by sex, such factors differ considerably between the sexes, most notably for lung cancer, but also for major gastrointestinal and urinary organs for which SEER baseline rates for males are well in excess of those for females. There is uncertainty here, but it cannot be quantified.

H. Dosimetry

The organ dose from external low-LET radiation can usually be estimated within a factor of 2 in individuals who wear film badges or other quantitative detection devices or who work in carefully monitored areas. The absorbed radiation dose is even more uncertain for any unbadged individual whose dose estimate depends on an environmental reading that may not be in his immediate vicinity, and is subject to attenuation by environmental shielding as well as body shielding and thus may vary over time. Exposure from ingestion or from sources absorbed within the body, such as iodine-131, thorotrast, radium, and radon daughters, is characterized not only by uncertainties as to level of dose, but also by the lack of precise information on their relative biological effectiveness. If the absorbed radioisotope is long-lived and can be measured in an individual and in specific organs, dose estimation may be much more accurate. The determination of iodine-131 doses to the thyroid after the fact, e.g., from weapons tests, will always be difficult in view of the indirectness of the exposure through the food chain and the physiological variables affecting the uptake of the radioisotope by the gland. A major effort, also mandated by PL 97-414, is currently in progress to address the radioiodine problem. The Working Group early determined that it should extend its PC estimation to internal emitters only where adequate epidemiological data were available, i.e., for radium-224 in relation to bone cancer.

The absorbed dose to the relevant tissue, generally an average over the target organ in the case of external radiation, is the quantity employed in these tables because this is the form in which BEIR III presented its risk estimates. These, in turn, were based on reports on the effects of diagnostic and therapeutic irradiation that generally state dose-specific risk estimates in terms of the tissue dose, and on reports on the A-bomb survivors whose external (kerma) doses were converted to tissue doses by means of Kerr's table (1). The relevant dose to a particular organ will, however, in many instances be difficult

to determine for such reasons as the following: (a) attenuation by overlying tissues will in general vary with photon energy; and (b) in the case of partial-body exposure, or whole-body exposure to highly directional radiation fields, calculation of a mean organ dose may be very uncertain. In the case of partial-body irradiation, the dose to an organ may be markedly non-uniform; this is especially true for an organ like the active bone marrow, which is widely distributed in the body. If the dose-response function were truly linear, it would be appropriate to utilize the average dose over the entire organ and, for small doses--of the order of 10 rad or less--linearity can be assumed. If, however, the maximum and minimum doses to different parts of the organ are very different, serious errors can result--in either direction. If the maximum dose is not too large, and the response function is linear-quadratic, then the "effective" dose will be under-estimated by the averaging process, but if the maximum dose is large enough to cause substantial cell sterilization, the "effective" dose can be over-estimated.

The quality of the dosimetry on which risk coefficients are based is best for series derived from therapeutic irradiation. Treatment plans are carefully made and usually recorded in a fashion that permits the calculation of doses, even to organs outside the primary radiation field. The dose estimates for diagnostic irradiation are more uncertain and can be difficult to reconstruct and describe with precision, e.g., in the case of fluoroscopy used to monitor artificial pneumothorax therapy for tuberculosis (16). Average values may be fairly accurate, but individual doses highly variable.

Because the dosimetry for the A-bomb survivors is now being revised (17,18), the age- and sex-specific risk estimates which depend on their experience are now uncertain. Various attempts have been made (19-21) to predict the extent to which the next generation of dose estimates will change previously calculated risk coefficients, and it appears that certain low-LET risk coefficients may be increased, but probably by no more than a factor of 2 (20). The types of cancer for which the co-efficients depend essentially on the A-bomb data are: leukemia and cancers of the esophagus, stomach, colon, lung, breast, bladder, and kidney. Sites for which the risk coefficients are relatively independent of the A-bomb data, at least as to level of risk, are: bone, salivary gland, liver, pancreas, and thyroid. Charles et al (22) recently reviewed the 1977 UNSCEAR report (2) to estimate the overall risk of radiogenic cancer based on all sources of human data except the experience of the A-bomb survivors. Their estimate also differs from current risk estimates by a factor of about 2.

The dosimetry for the British ankylosing spondylitis series (23), a major source of data for the calculation of risk coefficients, has been under investigation by a British team for some time but, except for leukemia, the only published estimates are the preliminary figures given in the BEIR III report (1).

A particularly difficult dose-reconstruction has been that for the thyroids of patients with tinea capitis treated with epilating doses of X rays in Israel (24). The attribution of excess thyroid cancer to an average tissue dose of about 9 rad has important implications for the

shape of the dose-response curve, but even a careful reconstruction with phantom simulation may not take full account of the influence of movement on the part of the patient during the therapeutic procedure, movement that might have led to higher doses to the thyroid than those estimated.

I. Coefficients Describing the Dependence of Risk on Dose

Although the risk coefficients are the most complex element in the PC calculation, it is doubtful whether they are subject to errors as large as those of most dose estimates for persons exposed to fallout, for example. Standard statistical measures of uncertainty calculated for specific data sets are meaningful when data are reasonably numerous, as is true for some sites in the case of A-bomb survivors, but such instances are few, and sampling variation is only one part of the uncertainty surrounding risk coefficients. As an example, Table VII-3 reproduces the linear regression estimates and 90 percent confidence intervals for many types of cancer mortality associated with ionizing radiation among A-bomb survivors (25). Only for leukemia, lung cancer, and breast cancer do the 90 percent limits differ from the mean by a factor less than 2. These coefficients are for all ages at exposure. When one confronts the task of calculating PC tables over the entire age range, one finds that it is only for leukemia, and cancers of the breast, bone, salivary glands, and thyroid, that there is enough experience upon which to base risk coefficients for those exposed under age 10. Most recorded series pertain to exposure during adult life, and even the A-bomb survivors exposed before age 10 provide very little information on the risk of radiogenic cancers of gastrointestinal, urinary, and respiratory organs. This is discussed more fully above in Section F.

It should be borne in mind that the site-specific risk coefficients for cancer incidence in the BEIR III report are, except for leukemia and bone cancer, linear coefficients. They were derived by the BEIR III committee as an adjunct to the mortality estimates, and represent the Committee's summary of the evidence from the medical and the environmental exposures reported in the literature as of 1979. In some instances incidence risk estimates were obtained by transforming mortality risk estimates as explained in the BEIR report (1). The technique employed the lifetime expectations of (a) developing, and (b) dying of, cancer of a specific site.

The conversion of BEIR linear-model risk coefficients to coefficients for the BEIR linear-quadratic model, in which the excess risk from an exposure to D rad is proportional to $D + D^2/116$, was accomplished by dividing the linear coefficients by 2.5 (see Chapter V-B). The results obtained by this procedure are not necessarily identical to those that would have been obtained by reanalyses of the original data using the new model, but this source of uncertainty is unimportant relative to that involved in the choice of the crossover dose of 116 rad. The statistical uncertainties underlying this procedure are appreciable. The reliability of the crossover value depends more on its agreement with experimental results obtained over a wide range of biologic systems than on its statistical stability (See Chapter V-B).

Finally, a question has been raised as to the source of the BEIR III coefficients, especially their considerable dependence upon the experience of the Japanese A-bomb survivors and their applicability to the U.S. population. The only available test here is one of consistency among sources, and in general the absolute risk coefficients obtained in Japan are very much like those obtained in the U.S. and U.K. except that their variances are smaller because the experience is larger. This subject is discussed more fully in Chapter III-K.

J. Dose Rate

The linear-quadratic model used for the risk estimates with low-LET radiation for all cancer other than breast and thyroid, having a "cross-over" point at 116 rad, is based on acute (i.e., fairly high dose rate) exposures to radiation. As has already been discussed in Chapter III, at low dose rates the quadratic term becomes less important, and at very low dose rates it is assumed that the dose-response function is reduced to the linear term only. The exact dose rate below which the quadratic term can be ignored is not precisely determined, but experimental studies indicate that it might be on the order of 0.001 rad/min or 1 rad/day, or perhaps somewhat greater (see Chapter III-I). For acute exposures below 5 rad, the contribution of the quadratic term is on the order of 4 percent or less of that of the linear term alone. The approach being suggested for the calculation of protracted or fractionated radiation (see Chapter V) will reduce any dose-rate effect to well within these limits of error. For thyroid and female breast the available data suggest a linear dose-response model which implies that there should be no influence from variation in dose rate. The latter inference is borne out in the case of the breast.

In human cells in vitro the greatest change in effect (cell inactivation) with dose rate occurs in the range 100 rad/min to 10 rad/hr (26); one may, therefore, as a first approximation, assume no variation in effect with dose rates in the LQ model at dose rates greater than 100 rad/min. For dose rates in the transition range (10 rad/hr to 100 rad/min), if one were to treat large exposures as acute doses, the margin of error would be the contribution of the quadratic term of the linear-quadratic model. Below the cross-over point (116 rad) that would imply a factor less than 2.0. It is reasonable to assume that not many exposures will fall in this dose-rate range, but such exposures should be treated on an ad hoc basis.

The uncertainty associated with the dose rate is essentially incorporated in the factor estimated for the choice of dose-response model, especially when account is taken of the uncertainty in the crossover dose.

K. Time-Response Models

Risk coefficients are either _absolute_, i.e., calculated as an excess over and above baseline incidence, or _relative_, i.e., expressed in multiples of the natural incidence. Absolute risks are frequently expressed as excess cases per million persons per year and per rad (or rem), whereas a

relative risk estimate may be some (generally constant) fraction of the baseline incidence corresponding to the effect of a fixed dose, e.g., a rad (or rem). When a constant absolute risk is used as a time-response model it suggests that the risk of radiogenic cancer is viewed as independent of the underlying baseline risk. A constant relative risk model for time-response is suggestive of mechanisms by which radiation interacts with other causes to multiply the baseline risk by some constant (see Chapter IV-H). These models, and the measures they generate, have very different implications for the calculation of excess cancers following exposure to radiation. Under the constant absolute risk model for distributing radiogenic cancers over time, once expression has been established, the excess per unit of population, dose, and time, is constant. Under the constant relative risk time-response model, the number of excess cases during the period of expression is a fixed multiple of baseline incidence and, therefore, for most solid tumors, increases with age. For the interval observation from which the risk estimates are generated, both measures must, of course, yield the same total excess, but the excess will be distributed differently over time. For the period beyond the interval of observation, the predicted excess will frequently be very different for the two measures and greater with the relative risk model since baseline rates of cancer generally increase markedly with age.

Although the absolute risk time-response model has dominated the literature and has been the choice of such groups as the ICRP (4) and UNSCEAR (2), in the NAS BEIR I (27) and BEIR III (1) reports it has been used in parallel with the constant relative risk time-response model. Recent data on the experience of the A-bomb survivors (25,28) have provided a strong basis for employing the relative risk model in preference to the absolute risk model, especially for breast cancer and lung cancer, and the working group has adopted the relative risk approach in calculating this first edition of the PC tables (see Chapter V-C). The use that is made of the constant relative risk approach, however, is not based on the assumption that the relative excess per rad is invariant with respect to age, sex, tumor site, geographic or cultural region, etc. Rather, it is limited to the assumption of a relative risk that is constant over the period 10-35 years after exposure for a particular tumor, a particular age-group at exposure, a particular sex, and a particular population level of baseline incidence.

Within the period of observation, generally up to 35 years after exposure, the uncertainty introduced by the choice between the two models is not large, but it does increase thereafter. In the life-time projections of the BEIR III report, where risks are extrapolated beyond the present range of the available human data, constant relative risk estimates of the total burden of radiogenic cancer from a continuous exposure of 1 rad/year beginning at birth are about 3 times those based on constant absolute risk estimates (1). With continuous exposure beginning at age 20, however, the differential in risk is only about two-fold.

The constant relative risk model is definitely superior to the constant absolute risk model which simply does not fit the data. But with additional observations, beyond the 35-year interval for which data are presently available, the constant relative risk model may fit less well than it does for the earlier period. For example, the multiple of baseline incidence may decline

after 40 or 50 years. Thus, PC estimates calculated for intervals of more than about 35 years after exposure have an additional element of uncertainty.

L. Interaction with Other Carcinogens

The prevalence of carcinogenic influences in one's environment and life-style suggests that any individual with cancer following exposure to ionizing radiation will also have been exposed to other carcinogens. The only competing risk factor for which the Working Group has been able to find adequately quantitative data is smoking in relation to lung cancer. Smoking is a very potent risk factor for lung cancer. The relative risk of lung cancer for heavy smokers versus non-smokers, about 24, is exceeded for very few risk factors. Unfortunately the literature is unclear as to the nature of the interaction between smoking and ionizing radiation in this case: a recent analysis of the experience of the U.S. uranium miners suggests a multiplicative relationship (29), another on Swedish iron miners suggests an additive relationship (30), and finally, the data on the A-bomb survivors suggest additivity (31). In the present report, additivity has been assumed for low-LET radiation and a multiplicative relationship for exposures to radon daughters. The range of uncertainty surrounding the choice of model in this case is roughly indicated by the values of "W" in Chapter IV-H that vary from 6.8 for non-smoking males to 0.29 for males with a two-pack-a-day habit. That is, these are the multipliers that are considered appropriate for the additive model, while under the multiplicative model "W" is one.

For many sites of cancer there are factors that seem able to increase the risk of cancer by a factor of two or more, and for all of these it has been assumed that the multiplicative model is more appropriate. This assumption, it should be noted, is not based, as is the choice of model for smoking, on empirical studies of radiation and other specific carcinogens, but on the fact that, in the few series with relevant observations, the distribution of the radiogenic excess over time appears to be proportional to baseline incidence. If another carcinogenic factor is present in addition to the radiation, and to a degree greater than average for the baseline population, and the two factors are additive in effect, the normal cancer incidence assumed for the PC calculation is too low and the resulting PC value, too high. If, on the other hand, they interact multiplicatively, no adjustment is required. The problem is discussed further in Chapter IV.

M. Other Sources of Uncertainty

In addition to the above sources of uncertainty, for which there is some information, others can be named for which information is completely lacking: hormonal status, genetic or other differences in DNA repair capability, and other host factors, particularly immune status. It is extremely difficult to establish the etiology of an individual tumor, but epidemiologic and toxicologic studies have identified a number of specific carcinogens for man, and any instance of a cancer following exposure to ionizing radiation should ideally be reviewed in the context of exposures to other carcinogens that may, in fact, have been responsible for initiating

the tumor. Assigning to each known carcinogen its share of responsibility in the process, however, requires far more information than is presently available in quantitative form, and the Working Group has been able to go no farther in this direction than to account for the influence of smoking status in instances of lung cancer (see Chapter VI-H). The PC calculations are unaffected, however, by exposure to carcinogens which interact multiplicatively with ionizing radiation. Finally, if completeness of ascertainment for slowly progressing tumors, like thyroid cancer, has been greater for exposed subjects than for the general population, an upward bias is introduced into any PC calculation.

N. Effects of Variation in Density of Energy Deposition (LET)

The above discussion has dealt largely with low-LET radiation. There are, however, two exceptions: the tables for bone cancer apply only to alpha radiation from radium-224, and tentative estimates have been provided for lung cancer following exposure to alpha particles from inhaled radon daughters. Data on the induction of bone cancer by low-LET radiation are inadequate as a basis for PC estimation and the Working Group, following the BEIR III report, has used the medical experience with radium-224 as a basis for PC estimation, but with no intention that it be applied to the long-lived isotopes of radium much less to low-LET radiation. This means that the bone tables are of very restricted applicability.

Although the Working Group has assumed, throughout, that X and gamma radiation are equivalent in terms of RBE, this is not strictly so since the LET and, therefore, generally the RBE for any given type of radiation, will diminish as the energy is increased. For this reason, energetic gamma radiation is less effective than 250kVp X rays. The difference is relatively small at higher doses and dose rates, but may be quite significant at low doses and dose rates. For example, for mutations in Tradescantia and chromosome aberrations in animal cells, cobalt-60 gamma radiation at low doses was observed to be between 1/3 to 1/2 as effective as the reference 250kVp X radiation (32,33). This implies that at low doses and dose rates exposures to energetic gamma radiation is less damaging than exposure to so-called ortho-voltage X rays and that the tables will yield PC's in excess of the true values. It also implies that, insofar as some of the site-specific risk factors derive in part from the Hiroshima-Nagasaki experience, these risk factors may be somewhat lower than they would for kVp X rays. The Working Group does not have the data that would allow it to address this issue at the computational level.

O. Propagation of Uncertainties and Their Effect upon the Probability of Causation

Table VII-6 summarizes the various sources of uncertainty, how they were handled, their estimated magnitude and how their resolution by the Working Group may have influenced the PC values that can be calculated from the procedures detailed here. It is desirable to estimate the effect that these uncertainties, acting jointly, may have on the calculated value of the PC.

The excess relative risks are considered to be subject to uncertainties that have lognormal distributions. The logarithms of the "best estimates" which are tabulated then correspond to the mean values of normal distributions.

A normal distribution is symmetric about its mean, and deviations from that mean are expressible in standard form as multiples of the standard deviation of the distribution. Thus, for example, 95% of a normal distribution with mean μ and standard deviation σ lies between $\mu - 1.96\sigma$ and $\mu + 1.96\sigma$. A lognormal distribution also is symmetric about its geometric mean G, but in a multiplicative sense. G is the exponential of the arithmetic mean on the logarithmic scale. Defining the "geometric standard deviation" (G.S.D.), S, as the exponential of the standard deviation on the logarithmic scale, it follows, for example, that 95% of the distribution lies between

$$L = G \times S^{-1.96} = \exp(\ln G - 1.96 \ln S)$$

and

$$U = G \times S^{1.96} = \exp(\ln G + 1.96 \ln S).$$

In the above formulation, if G and S are estimated, then the interval (L,U) corresponds approximately to a 95% confidence interval for the true geometric mean. In some applications no value of S may be obtainable directly from data, but if a 95% "credibility interval" of the form (L,U) can be constructed for the true geometric mean, a subjective estimate for S can be calculated by solving the relationship

$$L/U = S^{3.92}.$$

The G.S.D. for a lognormally distributed estimate G, which is itself the product of K independent estimates, each with G.S.D. S_i, can be calculated as

$$\ln^2 S = \ln^2 S_1 + \ldots + \ln^2 S_K,$$

and a credibility interval for the true value can be calculated in terms of G and S.

Where G.S.D.s could be calculated from available data, as for variation in baseline rates, the values S_i were estimated as the exponentials of the standard deviations of the logarithms of the rates. In other instances the values of S_i were estimated as described above, relying on estimates of U and L.

The uncertainties are of two kinds: Those which may equally well be in either direction and those, like that which derives from the reassessment of the A-bomb dosimetry, which are considered more likely to be in one direction than the other. We refer to them briefly as unbiassed and biassed uncertainties.

1. Unbiassed uncertainties

o Baseline values. The All Areas SEER incidence rates are appropriate for an average member of the population of the United

States; a different baseline rate may, however, apply to a parti-
cular individual, based on geography of residence. Table VII-1
shows, for each of the ten SEER areas, the age-adjusted incidence
rate for each cancer. Geometric standard deviations (G.S.D.s) of
the rates have been calculated for each cancer for males and females
separately; they ranged from a low of 1.076 for acute leukemia in
males to a high of 1.636 for liver cancer in males. In general, the
G.S.D.s for particular cancers were of similar magnitude for males
and females. Upon pooling the G.S.D.s for cancers for which the
values were similar, the following values were obtained:

Kind of Cancer	Geometric Standard Deviation among SEER Registries S_i
All leukemia except chronic lymphatic	1.10
Acute or chronic granulocytic leukemia, bone, breast, pancreas, colon and kidney and bladder	1.17
Salivary glands, thyroid, lung and stomach	1.36
Esophagus and liver	1.53

o <u>Influence of Age at Exposure</u>. Risk estimates have been
provided for only those ages at exposure for which adequate data
are available. From Table VI-1 it can be seen that for most
cancers excess risk per rad varies by a factor of about 4 as
between ages 20-34 and 50+. Exceptions are leukemia, liver,
breast and thyroid cancer. Taking account of the stepwise
nature of the age variations shown in Table VI-1, a total un-
certainty of about 50 percent is suggested. If U and L are
estimated as 1.5 and 0.667 times the stated values, then U/L =
2.25, and the G.S.D. is calculated as $S_i = 1.23$.

o <u>Time Response</u>. As explained in Chapter V, a wave-
like, lognormal functional form has been used to express the
time course following exposure for radiation-induced leukemia
or bone cancer. For all other cancers, following an initial
latent period, relative risks per rad are assumed to be constant.
It is unlikely that the time course for leukemia is in error by
more than about two years - that is, the peak year for chronic
granulocytic leukemia is estimated to be five years after
exposure; the body of data concerning human radiation leukemo-
genesis is sufficiently large and consistent that an error of
more than two years in the timing of that peak is most unlikely.
The temporal distribution curve following exposure (Table X-
1-A) shows that an error of two years in the placement of the
curve seldom changes the value of the curve by much more than
10 percent, and amounts to about 20 percent as between three

and five years after exposure. The G.S.D. can be estimated, then, to be no more than 1.10.

With respect to the solid cancers, the Working Group has adopted the constant relative risk time projection model. Available data indicate that this model is at least an excellent first approximation; there may, however, be some variation with time in the relative risk, especially for persons young at the time of exposure, and after intervals of twenty-five to thirty years. Such uncertainty is assessed to be no more than a factor of about 1.3; the G.S.D. is estimated as 1.15.

o **Ratio of the Linear Coefficients in the Linear (L) and Linear-Quadratic (LQ) Dose-Response Models.**
As explained in Chapter V, the 1980 BEIR regression analyses of mortality from all forms of cancer except leukemia yielded coefficients in the ratio of 2.5. That is,

$$E_L/E_{LQ} = 2.5.$$

This ratio depended on the assumed crossover dose of 116 rad, an estimate derived from the data on mortality from leukemia. Had a different cross-over value been selected, a different ratio would have resulted. The ratio depends on the cross-over dose, C, as follows:

$$E_L/E_{LQ} = 1 + 174/C.$$

The consequences of assuming that C is as small as 33 rad, or as large as infinity, in alternative fits to the original data of the BEIR Committee, are shown below:

Cross-over Value C (rad)	Ratio E_L/E_{LQ}
33	6.3
50	4.5
75	3.3
116	2.5
200	1.9
Infinity	1.0

The formula for the "effective" dose is $D + D^2/C$ and thus effective dose varies little with the value C if the dose is less than 5 rad, but uncertainty in the linear term, 2.5, illustrated above, strongly affects the PC.

It is thought that the true value of the cross-over dose

is almost certainly in the range from 33 rad to infinity. The ratios which correspond to those values are 6.3 and 1, with a geometric mean of 2.5. If the probability that the stated range does cover the true value is assessed at 99%, then the G.S.D. for the ratio is $1.43 = 6.3^{1/5.12}$. This value applies to all cancers except breast cancer and thyroid cancer, for which a linear dose response model has been used.

An infinite cross-over value, which corresponds to the value of 1.0 for the ratio E_L/E_{LQ}, characterizes the linear dose-response model. The pure quadratic dose response model would correspond to a cross-over value of zero rad, and an infinite ratio. Even for a cross-over value as low as 33 rad, the dose-squared term adds no more than 15 percent to the effective dose for an organ dose of 5 rad.

2. Biassed Uncertainties

o Latent Period. There seems little doubt that beyond 15 years from exposure, the full radiation risk applies for all cancers except leukemia and bone cancer and that at least five years is required for a radiation exposure to result in an overt cancer. The Working Group has chosen to calculate PC's on the assumption that full expression occurs as early as 10 years after exposure and has assumed that risk rises in a smooth way from the fifth to the tenth year. While there is little reason to question the estimates on the basis of latent period except in the interval 5 to 14 years, within that interval uncertainty does exist. This uncertainty is biassed, in the sense that the estimates, if erroneous, are likely to be erroneously high. If it be supposed that, in the interval 5 to 15 years, the risk estimate is, with credibility 95 percent, between one-half of that embodied in the Working Group's formula, and the full value, then the range .50 to 1.00, with geometric mean 0.71 (bias correction factor) has a G.S.D. of 1.19.

o Risk Coefficients. Many, but not all, of the risk coefficients used here are based mainly upon the experience of the Japanese A-bomb survivors; the exceptions are for cancers of bone, salivary glands, liver, pancreas, and thyroid gland. Recently it has become apparent that the dosimetry system, designated T-65, upon which the Japanese data are based, was seriously in error (34-36). An intensive effort to provide a new and better dosimetry system is under way (37,38) but has not yet been completed at this time (December, 1984). Estimates have been provided, however, of the changes that may result in the dose-effect coefficients for gamma rays, by Fujita as increases by a factor of 1.2 to 1.7 (39) and by Jablon as 1.6 to 2.2 (40). If it is assumed that a 95 percent credibility interval on the factor ranges from 1.2 to 2.2, the geometric mean would be 1.62, with a G.S.D. of 1.17. These values would apply only to those cancers for which the BEIR III risk estimates were based, in large part, upon the A-bomb survivor experience: the leukemias and cancers

of the esophagus, stomach, colon, lung, breast and kidney and bladder.

In addition to the uncertainty which results from prospective revision of the A-bomb dosimetry, additional uncertainty follows from the fact that the low-LET radiations in that situation were high-energy gamma rays, while 250kVp X rays, in experimental situations, have been reported to be more effective by a factor of 2 or 3 at doses on the order of two or three rad (32,41,42). This will not affect the use of the tables in cases where the radiations in question are hard gamma rays, as for workers in nuclear power plants or persons present at tests of nuclear weapons.

3. Combined Uncertainty

Recapitulating the uncertainties, and combining them, we have:

Source	G.S.D.(S_i)
Baseline values	
Esophagus and liver cancer	1.53
Salivary glands, thyroid, lung & stomach cancers	1.36
All leukemia except chronic lymphatic	1.10
All other cancers	1.17
Effect of age at exposure	1.23
Time responses	
Leukemia & bone cancer	1.10
Other cancers	1.15
Ratio of the L to LQ linear coefficient (Except breast & thyroid cancer)	1.43
Latent period (years 5-14 after exposure only) (Except leukemia and bone cancer) with bias correction factor = 0.71	1.19
Risk coefficients derived from A-bomb survivors Leukemia, cancers of esophagus, stomach, colon, lung, breast, kidney & bladder with bias correction factor = 1.62	1.17
Risk coefficients for other tabulated cancers	1.17

The combined uncertainties for each form of cancer are shown in Table VII-7.

4. Effect of Uncertainty of Risk upon the Probability of Causation

To obtain a 90 percent "credibility interval" for the PC

we first obtain limits for the value of R in the formula:

$$PC = R/(1 + R).$$

If upper and lower limits on R are substituted in this formula corresponding limits on the PC are obtained.

Suppose R is multiplied by some factor, V, giving

$$R' = R \times V.$$

If PC' is the "true" value of the PC which corresponds to R', then

$$PC' = R \times V/(1 + R \times V).$$

The value of PC' can be expressed directly in terms of PC and V as:

$$PC' = V \times PC/(1 + PC \times (V - 1)). \qquad \text{Eq. (1)}$$

Note that in Eq. (1) the PC is expressed as a fraction, rather than a percent.

The upper limit of the 90 percent "credibility" interval for R is obtained by multiplying the value of R by $S^{1.645}$; the corresponding lower limit is obtained by multiplying by the reciprocal of that value. Both limits must then be multiplied by the "bias factor" if it is different from 1.0.

For example, for bone cancer the value of S is 1.57 (Table VII-7). Raising this to the power 1.645 gives the result 2.10. The 90 percent credibility limits on R, for bone cancer, are obtained by multiplying by 2.10 and its reciprocal, 0.48. For All Leukemia the value of S is 1.59 which, when raised to the power 1.645 yields 2.14. For leukemia, however, the bias factor 1.62 applies, so the upper and lower limit factors must be multiplied by 1.62, yielding 3.47 and 0.76. These values can be used for V in Eq. (1) to obtain the 90% limits that correspond to any calculated PC. For bone cancer and All Leukemia, respectively, the 90% limits for a PC calculated as 5% would be

Bone cancer	2% to 10%
All leukemia except CLL	4% to 15%

The bounds for leukemia are quite asymmetrical because of the bias correction factor.

Table VII-8 shows, for each cancer, the factors V to be used to obtain lower and upper limits for the 90% credibility interval on any PC.

Table VII-9 shows for certain PC values and factor V values the corresponding lower and upper limits for the 90% credibility interval on the PC. As examples:

Acute leukemia – PC is calculated as 10%. From Table VII-8 the lower and upper factors are 0.74 and 3.55. From Table VII-9 the bounds on the credibility interval are 7% to 29%.

Breast cancer – PC at 15 or more years post-exposure is calculated as 5%. The factor bounds (Table VII-8) are 0.93 and 2.82. The bounds on the credibility interval (Table VII-9) are 5% to 13%.

Table VII-10 shows the calculated PC for which (with 95% credibility) the "true" PC is more than 50%. For example, from Table VII-8 it is found that for acute leukemia, the factor for the lower limit is 0.74. From Table VII-10 it is found that the value of the calculated PC, for which the "true" PC is at least 50%, with credibility 0.95, is between 56% and 59%. Exact calculation inverting Eq. (1) shows the value to be 57%.

In summary, although the effect of uncertainty is somewhat variable depending upon the particular cancer and the latent period, certain generalizations can be made:

1. If the PC as calculated here is 2% or less, the "true" PC almost surely would be 7% at most (upper limit) even if we had sure knowledge concerning all the unknowns which contribute to the uncertainties.

2. If the PC is in the range of 5 to 10% the "true" PC might be quite small (1%), but might be as large as 30%.

3. If the PC is calculated to be at least 20%, the "true" PC is most unlikely to be less than 5% and may be as large as 40%.

REFERENCES - Chapter VII

1. Committee on the Biological Effects of Ionizing Radiation, "The
    Effects on Populations of Exposure to Low Levels of Ionizing Radiation:
    1980." National Academy Press, Washington, D.C., 1980.

2. United Nations Scientific Committee on the Effects of Atomic Radiation,
    "Sources and Effects of Ionizing Radiation." Report to the General
    Assembly Publ. E771X1, United Nations, New York, 1977.

3. U.S Interagency Task Force on the Health Effects of Ionizing Radiation,
    "Report of the Work Group on Science, June 1979." Office of the Sec-
    retary, U.S Dept of Health, Education and Welfare, Washington, D.C.,
    1979.

4. ICRP Publication 26, Annals of the ICRP, "Recommendations of the
    International Commission on Radiological Protection." Pergamon
    Press, Oxford, 1977.

5. Ron, E. and Modan, B., Thyroid and Other Neoplasms Following Child-
    hood Scalp Irradiation. In "Radiation Carcinogenesis: Epidemiology
    and Biological Significance" (J. D. Boice, Jr., and J. F. Fraumeni, Jr.,
    Eds.), pp. 139-151. Raven Press, New York, 1984.

6. Coleman, M., Kirsch, M. and Creditor M., Tumors Associated with
    Medical X-ray Exposure Therapy in Childhood. In "Late Biological
    Effects of Ionizing Radiation," Proceedings of a Symposium,
    Vienna, 1978, pp. 167-179, International Atomic Energy Agency,
    Vienna, 1978.

7. Young, J. L., Percy C. L. and Asire, A. J. (Eds.), "Surveillance,
    Epidemiology, and End Results. Incidence and Mortality Data: 1973-1977,"
    NCI Monogr. 57. U.S Govt Prtg. Off., Washington, D.C., 1981.

8. Cutler, S. J. and Young J. L. (Eds.), "Third National Cancer Survey:
    Incidence Data," NCI Monogr. 41. U.S. Govt. Printing Office, Washington,
    D.C., 1975.

9. McKay F. W., Hanson, M. R., and Miller, R. W., "Cancer Mortality in
    the United States: 1950-1977," NCI Monogr. 59. U.S. Govt. Printing
    Office, Washington, D.C., 1982.

10. Stewart, A. M., Leukaemia and Prenatal X-rays. Br. Med. J. 2:
    1381-1382 (1960).

11. Monson, R. R. and MacMahon, B., Prenatal X-ray Exposure and Cancers
    in Children. In "Radiation Carcinogenesis: Epidemiology and
    Biological Significance" (J .D. Boice, Jr, and J. F. Fraumeni, Jr.,
    Eds.), pp 97-105. Raven Press, New York, 1984.

12. Oppenheim, B. E., Griem, M. D., and Meier, P., Effects of Low-dose
    Prenatal Irradiation in Humans: Analysis of Chicago Lying-in Data
    and Comparison with other Studies. Radiat. Res. 57: 508-544 (1974).

13. Jablon, S. and Kato, H., Childhood Cancer in Relation to Prenatal Exposure to Atomic-bomb Radiation. Lancet 2: 1000-1003 (1970).

14. Baum, J. W., Population Heterogeneity Hypothesis on Radiation Induced Cancer. Health Phys. 25: 97-104 (1973).

15. Beebe, G. W., Kato, H., and Land, C. E., Studies of the Mortality of A-bomb Survivors. 6. Mortality and Radiation Dose, 1950-1974. Radiat. Res. 75: 138-201 (1978).

16. Boice, J. D., Rosenstein, M., and Trout, E. D., Estimation of Breast Doses and Breast Cancer Risk Associated with Fluoroscopic Chest Examinations of Women with Tuberculosis. Radiat. Res. 73: 373-390 (1978).

17. Bond, V. P. and Thiessen, J. W. (Eds.), "Re-evaluations of Dosimetric Factors, Hiroshima and Nagasaki," Department of Energy Symposium Series No. 55, (CONF-810928). U.S. Govt. Prtg. Off., Washington, D.C., 1982.

18. Sinclair, W. K., Revisions in the Dosimetry of the Atomic Bomb Survivors. In "Radiation Research, Reviews and Summaries on Chemistry, Physics, Biology and Medicine," Proceedings of the Seventh International Congress of Radiation Research, July, 1983, (J. J. Broerse, G. W. Barendsen, H. B. Kal, and A. J. van der Kogel, Eds.) pp. 63-73. Martinus Nijhoff Publishers, Amsterdam, 1983.

19. Dobson, R. L. and Straume, T., Estimated Cancer Risks and Neutron RBE's from Revised Hiroshima and Nagasaki Dosimetry. Br. J. Radiol. 55: 788-795 (1982).

20. Fujita, S., Awa, A. A., Pierce, H., Kato, H., and Shimizu, Y., Re-evaluation of the Biological Effects of Atomic Bomb Radiation by Changes of Estimated Dose. In "Biological Effects of Low-Level Radiation," Proceedings of a Symposium, Venice, April 11-15, 1983, pp. 55-60. International Atomic Energy Agency, Vienna, 1983.

21. Sinclair, W. K. and Failla, P., Dosimetry of Atomic Bomb Survivors, Radiat. Res. 88: 437-447 (1981).

22. Charles, M. W., Lindop, P. J., and Mill, A. J., Pragmatic Evaluation of Repercussions for Radiological Protection of Recent Revision in Japanese Abomb Dosimetry. In "Biological Effects of Low-Level Radiation," Proceedings of a Symposium, Venice, April 11-15, 1983, pp. 66-75. International Atomic Energy Agency, Vienna, 1983.

23. Smith, P. G., and Doll, R., Mortality among Patients with Ankylosing Spondylitis after a Single Treatment Course with X-rays. Br. Med. J. 284: 449-460 (1982).

24. Ron, E. and Modan, B., Benign and Malignant Thyroid Neoplasms after Childhood Irradiation for Tinea Capitis. J. Natl. Cancer Inst. 65: 7-11 (1980).

25. Kato, H. and Schull, W. J.: Studies of the Mortality of A-bomb Survivors. 7. Mortality, 1950-1978: Part 1. Cancer Mortality. Radiat. Res. 90: 395-432 (1982).

26. Hall, E. J., Radiation Dose Rate: A Factor of Importance in Radiobiology and Radiotherapy. Br. J. Radiol. 45: 81-97 (1972).

27. National Academy of Sciences Advisory Committee on the Biological Effects of Ionizing Radiation: "The Effects on Populations of Exposure to Low Levels of Ionizing Radiation." National Academy of Sciences-National Research Council, Washington, D.C., 1972.

28. Land, C. E. and Tokunaga, M. Induction Period. In "Radiation Carcinogenesis: Epidemiology and Biological Significance" (J. D. Boice, Jr., and J. F. Fraumeni, Jr., Eds.), pp. 421-436. Raven Press, New York, 1984.

29. Whittemore, A. S., and McMillan, A., Lung Cancer Mortality among U.S. Uranium Miners. J. Natl. Cancer Inst. 71: 489-499 (1983).

30. Radford, E. P. and St. Clair Renard, K. G., Lung Cancer in Swedish Iron Miners Exposed to Low Doses of Radon Daughters. N. Engl. J. Med. 310: 1485-1494 (1984).

31. Blot, W. J., Akiba, S., Kato, H., Ionizing Radiation and Lung Cancer: A Review Including Preliminary Results from a Case-control Study among A-bomb Survivors. In "Atomic Bomb Survivor Data: Utilization and Analysis," (R. L. Prentice, and D. J. Thompson, Eds.), pp. 235-248. SIAM (Society for Industrial and Applied Mathematics), Philadelphia, 1984.

32. Bond, V. P., Meinhold, C. B., and Rossi, H. H., Low-dose RBE and Q for X-ray Compared to Gamma-ray Radiations. Health Phys. 34: 433-438 (1978).

33. Lloyd, D. C. and Purrott, R. J., Chromosome Aberration Analysis in Radiological Protection Dosimetry. Radiat. Tech. Dosimetry 1: 19-28 (1981).

34. Loewe, W. E. and Mendelsohn, E., Revised Dose Estimates at Hiroshima and Nagasaki. Health Phys. 41: 663-666 (1981).

35. Loewe, W. E., Revised Estimates of Neutron and Gamma-ray Doses at Hiroshima and Nagasaki. In "Reevaluations of Dosimetric Factors, Hiroshima and Nagasaki," (V. P. Bond and J. W. Thiessen, Eds.), pp. 25-47. Technical Information Center, U.S. Department of Energy Symposium Series No. 55 (CONF-810928). U.S. Govt. Prtg. Off., Washington, D.C., 1982.

36. Kerr, G. D., Findings of a Recent Oak Ridge National Laboratory Review of Dosimetry for the Japanese Atom-bomb Survivors. In "Reevaluations of Dosimetric Factors, Hiroshima and Nagasaki," (V. P. Bond and J. W. Thiessen, Eds.), pp. 52-95. U.S. Department of Energy Symposium Series No. 55 (CONF-810928). U.S. Govt. Prtg. Off., Washington, D.C., 1982.

37. Radiation Effects Research Foundation, "U.S. Japan Joint Workshop for Reassessment of Atomic Bomb Radiation Dosimetry in Hiroshima and Nagaskai" Proceedings of a Workshop Held at Nagasaki, Japan, February 16-17, 1983.

38. Radiation Effects Research Foundation, "Second U.S. Japan Joint Workshop for Reassessment of Atomic Bomb Radiation Dosimetry in Hiroshima and Nagasaki", Proceedings of a Workshop Held at Hiroshima, Japan, November 8-9, 1983.

39. Fujita, S., Potential Additional Data Sources for Dosimetry and Bio-logical Re-evaluation. In "Atomic Bomb Survivor Data: Utilization and Analysis," pp. 183-193. SIAM (Society for Industrial and Applied Mathematics), Philadelphia, 1984.

40. Jablon, S., Characteristics of Current and Expected Dosimetry. In "Atomic Bomb Survivor Data: Utilization and Analysis," pp. 143-152. SIAM (Society for Industrial and Applied Mathematics), Philadelphia, 1984.

41. NCRP Report No. 64, "Influence of Dose and its Distribution in Time on Dose-response Relationships for Low-LET radiations." National Council on Radiation Protection and Measurements, Washington, D.C., 1980.

42. Borek, C., Hall, E. J., and Zaider, M., X-rays May Be Twice as Potent as Gamma Rays for Malignant Transformation at Low Doses. Nature 301: 156-158 (1983).

Table VII-1

Age-Adjusted Annual Incidence Rates per 100,000
All Races Combined, SEER Data For 1973-1977

Males

| | Leukemia | | | Sali-vary | Thy-roid | Lung & Bronchus | Bones & Joints | Esopha-gus | Pan-creas | Sto-mach | Colon | Liver | Kidney & Bladder |
	Acute	Chronic Granulo-cytic	All*										
All Areas, except Puerto Rico	5.3	1.8	9.0	3.0	2.5	78.3	1.0	5.9	12.2	14.1	36.9	3.2	35.0
Connecticut	5.3	1.7	9.1	4.1	2.0	78.1	0.8	6.8	12.6	14.7	44.2	2.4	39.3
Detroit	4.4	2.1	12.0	3.1	2.3	86.6	0.8	7.8	12.0	15.1	37.6	3.4	35.3
Iowa	5.6	2.2	10.0	1.6	1.7	73.5	0.9	3.9	11.6	10.1	35.5	2.2	34.7
Atlanta	5.6	2.1	9.6	3.9	2.3	88.1	1.3	7.6	15.1	9.8	33.3	3.6	33.4
New Orleans	5.3	1.6	8.5	4.8	2.2	113.2	0.9	7.7	14.3	15.0	36.7	4.3	37.8
New Mexico	5.1	1.7	8.1	1.8	3.5	58.8	1.0	2.8	13.9	15.9	24.0	2.9	28.2
Utah	5.2	1.4	9.0	2.0	2.1	41.8	1.0	3.0	9.3	10.4	26.8	1.2	29.1
Seattle-Puget Sound	5.1	1.8	8.7	2.8	2.1	80.3	1.2	4.2	11.3	12.1	35.5	2.3	38.4
San Francisco-Oakland	5.8	1.4	9.0	3.6	3.1	83.2	1.1	6.2	13.1	15.7	39.9	4.2	34.8
Hawaii	5.5	1.8	8.3	2.1	6.2	62.4	1.2	7.4	10.9	30.2	32.6	8.5	24.6

* Excluding chronic lymphocytic leukemia.
** Non-Hodgkin's lymphoma plus multiple myeloma.

Table VII-1

Age-Adjusted Annual Incidence Rates per 100,000
All Races Combined, SEER Data for 1973-1977

Females

	Leukemia			Sali-vary	Thy-roid	Lung & Bronchus	Bones & Joints	Esopha-gue	Pan-creas	Sto-mach	Colon	Liver	Kidney & Bladder	Breast
	Acute	Chronic Granulo-cytic	All*											
All Areas, ex-cept Puerto Rico	3.7	1.1	5.7	1.2	5.5	22.2	0.6	1.9	8.0	6.4	31.3	1.3	11.4	85.4
Connecticut	4.0	0.9	6.1	1.1	4.4	21.8	0.6	2.2	8.7	7.0	35.8	1.2	12.7	91.8
Detroit	3.1	1.2	5.5	1.1	5.3	22.7	0.5	2.3	7.8	6.5	29.0	1.5	12.0	81.7
Iowa	3.5	1.3	5.8	0.9	4.2	14.6	0.7	1.1	6.9	4.2	34.5	1.1	10.8	80.6
Atlanta	3.9	1.1	5.7	1.2	6.3	21.5	0.8	1.7	8.2	5.1	29.6	1.1	10.0	87.3
New Orleans	3.1	1.3	5.0	1.2	4.6	27.5	0.6	1.5	9.3	6.8	29.1	1.4	12.3	76.2
New Mexico	2.8	1.0	4.9	1.0	6.6	21.3	0.6	1.4	10.3	7.6	....	2.2	10.5	75.6
Utah	3.2	1.5	5.7	0.9	6.5	8.5	0.9	0.5	5.9	4.8	22.8	1.1	9.4	74.7
Seattle-Puget Sound	4.0	0.7	5.6	1.6	4.6	26.5	0.7	1.6	7.2	5.3	31.2	1.0	11.8	89.3
San Francisco-Oakland	4.2	0.8	5.9	1.7	6.9	29.8	0.6	2.6	8.9	7.5	32.6	1.3	11.1	96.0
Hawaii	4.5	0.8	6.1	1.4	10.5	25.1	0.4	1.6	7.0	14.8	23.0	3.2	8.5	70.6

* Excluding chronic lymphocytic leukemia.
** Non-Hodgkin's lymphoma plus multiple myeloma.

Table VII-2

Largest and Smallest Ratios of Individual Registry Age-Adjusted
Cancer Incidence Rates to All Areas Rate

Site	Males		Females	
	Largest Ratio	Smallest Ratio	Largest Ratio	Smallest Ratio
Leukemia				
Acute	1.09 (San Francisco)	0.83 (Detroit)	1.22 (Hawaii)	0.76 (New Mexico)
Chronic Granulocytic	1.22 (Iowa)	0.78 (Utah)	1.36 (Utah)	0.64 (Seattle and Puget Sound)
All Forms*	1.33 (Detroit)	0.90 (New Mexico)	1.07 (Hawaii)	0.86 (New Mexico)
Bones & Joints	1.3 (Atlanta)	0.8 (CT & Detroit)	1.5 (Utah)	0.7 (Hawaii)
Salivary	1.60 (New Orleans)	0.53 (Iowa)	1.42 (San Francisco)	0.75 (Iowa and Utah)
Esophagus	1.32 (Detroit)	0.47 (New Mexico)	1.37 (San Francisco)	0.26 (Utah)
Stomach	2.14 (Hawaii)	0.70 (Atlanta)	2.31 (Hawaii)	0.66 (Iowa)
Colon	1.20 (Connecticut)	0.65 (New Mexico)	1.14 (Connecticut)	0.73 (Utah)
Liver	2.7 (Hawaii)	0.4 (Utah)	2.5 (Hawaii)	0.8 (Seattle and Puget Sound)
Pancreas	1.24 (Atlanta)	0.76 (Utah)	1.29 (New Mexico)	0.74 (Utah)
Lung & Bronchus	1.45 (New Orleans)	0.53 (Utah)	1.34 (San Francisco)	0.38 (Utah)
Breast	----	----	1.12 (San Francisco)	0.83 (Utah)
Thyroid	2.48 (Hawaii)	0.68 (Iowa)	1.91 (Hawaii)	0.76 (Iowa)

* Excluding chronic lymphocytic leukemia.

Table VII-3

Absolute Risk Coefficients for Fatal Radiogenic Cancers Among A-Bomb Survivors by Site or Type of Cancer

Site or Type of Cancer	Risk Coefficient[a]
Leukemia	1.72 (1.57, 1.87)
Esophagus	0.16 (0.02, 0.30)
Stomach	0.79 (0.34, 1.24)
Colon	0.30 (0.16, 0.43)
Lung	0.61 (0.37, 0.86)
Breast[b]	0.50 (0.29, 0.72)
Urinary tract	0.15 (0.04, 0.26)

[a]Excess deaths/10^6 person-year-rad; linear coefficients with 90% confidence intervals.

[b]Females only

From Kato and Schull, 1982 (25)

Table VII-4

Numbers of Deaths from Cancers of Various Organ Systems, 1950-
1974, in A-bomb Survivors under Age 10 in 1945.

	Number of Deaths	
	Total	With 10+ Rad
All malignant neoplasms except leukemia	26	11
Digestive organs and peritoneum	16	5
Stomach	12	4
All other digestive organs combined	4	1
Trachea, bronchus and lung	0	0
Lymphatic and hematopoietic	3	1

Table VII-5

Numbers of Deaths from Cancers of Various Organ Systems, 1950–1974, in A-bomb Survivors Aged 10-19 in 1945.

	Number of Deaths	
	Total	With 10+ Rad
All malignant neoplasms except leukemia	128	45
Digestive organs and peritoneum	70	21
Stomach	44	11
Colon	3	2
Esophagus, rectum and pancreas	7	3
Other digestive organs	16	5
Trachea, bronchus and lung	5	2
Breast	14	11
Lymphatic and hematopoietic	7	3
All other combined	32	8

Table VII-6

Summary of Uncertainties and the Effect of Their
Resolution on PC Values

Source of Uncertainty	Resolution by the Working Group	Practical Effect on PC Calculations
Dose to individual	Outside purview of Working Group	Highly variable, especially if unbadged
Source tables on cancer incidence	SEER tables for all races and regions combined, but specific by age and sex; only 1973-1981 data used	Without further adjustment for ethnic and regional differences, PC values may be high, or low; ignoring changes in incidence over time affects some PC's for early onset of certain cancers
Influence of age at exposure	Many coefficients for younger ages omitted; interpolation is necessary to obtain values for single years	Fewer PC values obtainable for younger ages; PC's for exposure after age 65 epecially uncertain
Sex differences	The few known sex differentials are used	Unknown
Sites and cell-types	Lymphomas and multiple myeloma excluded; liver, pancreas, salivary gland included	Exclusion makes PC approach inapplicable; inclusion may provide wrong guidance
Minimal latent period	Minimum of 2 years for leukemia and bone; smoothed 5-10 for solid	There will be fewer zero PC values within 10 years of exposure
Risk coefficients	BEIR III linear coefficients for solid tumors adapted to linear-quadratic model, except breast and thyroid	Essential statistical uncertainty carried forward into PC calculations
Dosimetry in epidemiologic studies	As reflected in the BEIR III coefficients	A-bomb revision may increase many risk coefficients by factor of 1.2-2.2 and PC values somewhat less

Table VII-6 (continued)

Source of Uncertainty	Resolution by the Working Group	Practical Effect on PC Calculations
Dose-response function	Linear-quadratic (LQ) model assumed for low-LET exposure, linear (L) for thyroid and breast	The true PC may be greater or less, depending on the actual form of the dose-response function. PC's calculated at less than 2% may be too large or too small by not more than a factor of 2.5, PC's of 5-20%, by not more than a factor of 2, and larger PC's, by lesser amounts
Dose-rate	Fractionated or continuous exposures within a 24-hour period are treated as single exposures. Other exposures separated in time are treated individually, not summed. Accumulations over longer periods are treated as separate exposures occurring on different days	Ignoring fractionation within a 24-hour period probably overestimates risk by an amount no greater than the quadratic coefficient multiplied by dose-squared. Under the linear model fractionation does not affect estimated risk
Time-response model	Constant relative risk model for solid tumors except bone; wave function for leukemia and bone	For leukemia and bone cancer, for which a wave function is clearly indicated, any uncertainty relates not to the choice of the model but to its precise form. For other tumors the effect on PC values depends on the interval between exposure and diagnosis and whether it falls outside the period of observation. Within the period of observation PC's will be lower toward the beginning of expression, and higher thereafter,

(continued)

Table VII-6 (continued)

Source of Uncertainty	Resolution by the Working Group	Practical Effect on PC Calculations
		than if based on the constant absolute risk model; after the period of observation PC's will be generally higher. Relative risk models incorporating some variation over time might increase or decrease particular PC estimates
Other risk factors	No adjustment made, except for smoking	Unknown, and depending on any interaction with radiation.

Table VII-7

Combined Uncertainties and Bias Correction Factors

Kind of Cancer	Years after Exposure	Combined Uncertainty (S)	Bias Correction Factor
All leukemia except CLL	Any	1.59	1.62
Acute or chronic granulocytic leukemia	Any	1.61	1.62
Bone	Any	1.57	1.00
Salivary gland	5-14	1.75	0.71
	15+	1.71	1.00
Esophagus	5-14	1.92	1.15
	15+	1.88	1.62
Stomach, lung	5-14	1.79	1.15
	15+	1.74	1.62
Colon, kidney and bladder	5-14	1.68	1.15
	15+	1.63	1.62
Liver	5-14	1.88	0.71
	15+	1.84	1.00
Pancreas	5-14	1.64	0.71
	15+	1.59	1.00
Breast	5-14	1.46	1.15
	15+	1.40	1.62
Thyroid	5-14	1.54	0.71
	15+	1.49	1.00

Table VII-8

Factors to be Used for Limits of a 90 Percent Credibility Interval

Kind of Cancer	Years after Exposure	Factor for Lower Limit	Upper
All leukemia except CLL	Any	0.76	3.47
Acute or chronic granulocytic leukemia	Any	0.74	3.55
Bone	Any	0.48	2.10
Salivary gland	5-14	0.28	1.78
	15+	0.41	2.42
Esophagus	5-14	0.39	3.36
	15+	0.57	4.58
Stomach, lung	5-14	0.44	3.00
	15+	0.65	4.03
Colon, kidney and bladder	5-14	0.49	2.70
	15+	0.73	3.62
Liver	5-14	0.25	2.01
	15+	0.37	2.73
Pancreas	5-14	0.31	1.60
	15+	0.47	2.14
Breast	5-14	0.62	2.14
	15+	0.93	2.82
Thyroid	5-14	0.35	1.44
	15+	0.52	1.93

Table VII-9

Limits for 90 Percent Credibility Intervals on Probabilities of Causation

Factor	PC =	(A) Lower Limits (95 percent)				
		5%	10%	20%	30%	50%
				Percent		
0.2		1	2	5	8	17
0.3		2	3	7	11	23
0.4		2	4	9	15	29
0.5		3	5	11	18	33
0.6		3	6	13	20	38
0.7		4	7	15	23	41
0.8		4	8	17	26	44
0.9		5	9	18	28	47

Factor	PC =	(B) Upper Limits (95 percent)				
		2%	5%	10%	20%	30%
				Percent		
1.4		3	7	13	26	38
1.6		3	8	15	29	41
1.8		4	9	17	31	44
2.0		4	10	18	33	46
2.2		4	10	20	35	49
2.4		5	11	21	38	51
2.6		5	12	22	39	53
2.8		5	13	24	41	55
3.0		6	14	25	43	56
3.2		6	14	26	44	58
3.4		6	15	27	46	59
3.6		7	16	29	47	61
3.8		7	17	30	49	62

Table VII-10

Values of the PC for which a 95 Percent

Lower Credibility Limit is 50 Percent

Factor for Lower Limit	PC for which 50% is the Lower Limit Percent
0.2	83
0.3	77
0.4	71
0.5	67
0.6	62
0.7	59
0.8	56
0.9	53

CHAPTER VIII - FUTURE REVISION OF THE TABLES

The tables cannot now provide precise measures of the probability that certain cancers have resulted from previous exposures to known doses of ionizing radiation. The tables represent, however, a first and important step in the direction of a rational basis for assigning to radiation exposure a measure of the likelihood of its role in the causation of individual cancers.

The PC tables will have to be revised periodically as new information and new insights become available. The Orphan Drug Act provides a criterion for the frequency of revision: every 4 years or whenever the Secretary of Health and Human Services "deems it necessary to ensure that they continue to represent the best available scientific data and expertise." The United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) has in preparation another of its periodic reports that is scheduled to include a section on carcinogenesis, the last such section having been published in the 1977 report. The National Academy of Sciences is forming a new committee that will first study the effects of high-LET radiation and then move on to low-LET radiation. In perhaps two years the revision of the dosimetry of the Japanese A-bomb survivors may have begun to yield revised risk estimates based on that experience. The BEIR III report was based on the world literature as it existed in 1979, and the mortality data on the A-bomb survivors at that time had been reported only through 1974. Their mortality through 1978 has now been reported and within a year or two there should be an update through 1982. These several efforts, at least, ought to be completed before any overall revision of the tables would seem useful, unless the effort to revise the tables were to duplicate those efforts.

On the other hand, it would be well to keep in mind the possibility that some portion of the data on which this first version of the tables rests may become obsolete before a general revision is indicated. In that event, a supplement might well be issued with respect to a particular site for which greatly improved estimates could be provided, or for a site excluded from the present report. Or, perhaps as a result of the initial deliberations of the new NAS Committee, it may be evident that estimates could be made for certain exposures to high-LET radiation. Another possible candidate for a supplement is a revision of the material on thyroid cancer to include the effects of exposure to internally deposited iodine-131 for which the Working Group concluded that PC estimates could not be made at this time. Section 7a of the Orphan Drug Act also provided for a study of the effect of iodine-131 on the likelihood of thyroid cancer, and an Ad Hoc Working Group on Thyroid/Iodine-131 Assessments has been formed to address this task.

The BEIR III report was not created with the needs of the radioepidemiologic tables in view and the Working Group has found that some of the factors developed in that report to enable estimates to be made for the effect of continuous exposure of the entire population from birth to the end of life lack the reliability needed for the present purpose (cf Chapter VII). The BEIR Report also provided no systematic basis for estimating the effects of exposure to internal emitters, a difficult subject at best and one for which few data adequate for PC estimation

exist. Internal emitters are important sources of exposure, especially
plutonium and radon daughters, and a comprehensive set of procedures for
PC calculations ideally should make provision for them. The NAS committee
preparing the next BEIR report should be sensitive to the need for
PC estimates and provide the kind of statistical information that is re-
quired for their calculation. If the Department of Health and Human
Services were to maintain a standing group charged with responsibility for
the tables, liaison between this group and the NAS committee will also be
necessary if supplements to the tables are to be issued as updates on
particular sites of cancer prior to any full-scale revision. A standing
committee might also observe the use of the PC tables in compensation
cases by the courts or by administrative boards and consider how the
tables might be improved for judicial use.

In brief, four or five years hence, authoritative information concern-
ing the radiation induction of solid tumors will be much improved from
its present state; not only will the data be more robust statistically in
consequence of larger numbers, but the data on A-bomb survivors, now
available only through 1978, will have been extended to 1982 or 1986.
Thus, it should be possible either to verify that the relative risk
time-response model applies to follow-up periods as long as 40 years, or
to learn what modifications are required; additional evidence concerning
the shape of the necessary dose-response curves should help to clarify
this controversial subject and data from other human studies may cast
additional light on the general applicability of risk estimates generated
from particular populations. Further, greater confidence in the appropriate-
ness and reliability of some of the key assumptions, especially those relat-
ing to dose-rate effect, dose-response model, and time-response model, will
depend on a better understanding of the mechanisms of malignant transformation
at the molecular and cellular levels where research is presently very active.

CHAPTER IX: THE GENERAL FORM OF THE PC CALCULATION

The probability of causation (PC) for a cancer diagnosed after one or more exposures to ionizing radiation has the general form, simplified from formula IV-2,

$$PC = R/(1 + R).$$

The relative excess, R, in the case of a single exposure of short duration to a subject typical of the US population, is given by the product of three quantities:

$$R = F \times T \times K.$$

In the above expression F quantifies the dependence of R on the radiation dose to the relevant tissue, and its quality. The use of a mere badge or environmental reading would lead to erroneous PC values; absorbed tissue dose must be used in the procedures described here. T gives the dependence of R on time after exposure. K indicates the dependence of R on age at exposure, sex, and, for some cancers, age at diagnosis.

For low-LET radiation, the exposure factor F depends only upon radiation dose D and whether the assumed dose-response function is linear or linear-quadratic. The value of F is presented below as a function of absorbed tissue dose (D), measured in rad, by cancer site and radiation quality:

Radiation Quality	Cancer Site		
	Bone	Thyroid or Breast	Other
Low LET	----	D	$D + D^2/116$
High LET	D	----	----

The above procedures are not intended to be used for cases involving exposure from internal emitters, with the exception of radium-224 in relation to bone cancer.

The factor $T = T(A_1,Y)$ represents the relative likelihood that a cancer induced by an exposure at age A_1 will be diagnosed after Y years (i.e., at least Y years but less than Y + 1 years). In this report both age and Y are integer-valued variables: a person exposed 17 years and 4 months after birth is considered to be 17 years old at exposure, and if a cancer is diagnosed 12 years, 11 months after exposure Y is considered to be 12 years.

Under the constant relative risk model, which has been used here for cancers other than leukemia and bone cancer, T depends only on Y, and this dependence is extremely simple (see Chapter V):

Y	0-4	5	6	7	8	9	10+
T(Y)	0	.074	.259	.500	.741	.926	1.000

The constant relative risk model has not been assumed to hold for leukemia and bone cancer. For these cancers T denotes the conditional probability, assuming that a cancer has been caused by an exposure at age A_1, that it will be diagnosed Y years later. T is calculated as the lognormal probability that a radiation-induced cancer is diagnosed between Y and Y + 1 years after exposure at age A_1. For bone cancer and chronic granulocytic leukemia, T depends only upon Y, while for acute leukemia and for leukemia generally, without regard to type, T depends upon exposure age A_1 as well as Y. T is tabulated separately in Chapter X for each of these sites, for integer values of Y between 0 and 49 and, where required, for A_1 between 0 and 75.

As noted in Table VI-1, the observational base for the risk co-efficients is generally no more than 30 or 35 years after exposure. The various specifications of T(Y) or $T(A_1,Y)$ for specific cancer sites invite application beyond the period of 30-35 years or so of follow-up that form the observational basis for the risk coefficients used in this report, and indeed this seems the most reasonable course to take if estimates must be made for cancer cases occurring long after exposure. But it should be recognized that we do not in fact have much information on the risk of radiation-induced cancer for periods beyond 35 years or so after exposure. Unpublished data on cancer mortality among A-bomb survivors through 1982 (H. Kato, personal communication) appear to be supportive of a continued increase in risk in absolute terms, a finding consistent with the constant relative risk model, and excess leukemia risk, which already had fallen to a level difficult to detect, remains low, as would be predicted according to a lognormal model for temporal distribution of risk. The fact remains, however, that making probability of causation estimates for cancers diagnosed more than 35 years or so after exposure involves projections in time beyond our present observational basis, and that there is more uncertainty involved in such projections as they are removed farther and farther in time from that observational basis.

The factor $K = K(A_1,A_2,S)$ is the relative excess at age A_2 for a person of sex S exposed at age A_1, when F = 1 and T = 1. For cancers other than leukemia and bone cancer K does not depend upon A_2 and is tabulated by site. For leukemia and bone cancer

$$K = E/I.$$

In this formulation $E = E(A_1,S)$ has the following theoretical interpretation: it is the estimated probability, for F=1, that a radiation-induced cancer will be diagnosed at some time after an exposure at age A_1, provided that no other cause of death intervenes. A quantity of more practical importance is T(Y) x E, which is the probability of cancer Y years after exposure, assuming survival to that year. $I(A_2,S)$ is the (site-specific) baseline cancer incidence for persons of age A_2 and sex S. E and I are tabulated separately for bone cancer and for each leukemia type considered.

It must be emphasized here, following the discussion in Chapter IV-E to G, that the use of the SEER values for baseline incidence presupposes that the calculation is being made for an individual who, apart from the particular radiation exposure of interest, is "typical" of the US population for his age and sex with respect to cancer risk. The only exceptions that are made here pertain to the smoking history of an individual with lung cancer (see Chapter IV-H) and to prior and unrelated exposure to ionizing radiation itself (see Chapter IV-E). It has not been possible to take into account atypical exposure to other carcinogens such as asbestos, for example, for which quantitative data adequate for the present purpose do not exist. Given an atypically high exposure to a known carcinogen other than ionizing radiation or cigarette smoking (in the case of lung cancer), which interacts additively with radiation exposure, it is clear that the bias in the calculated PC value would be upward. That is, if it were possible to take into account the influence of the other carcinogen, as is done for smoking in the case of lung cancer, the adjustment would increase the baseline incidence above the average SEER rate and thus reduce the PC value below that found by means of the tables presented in this report. The opposite would be true for an atypically low exposure. On the other hand, the other carcinogen might well interact multiplicatively with radiation, for example if the other agent acted by promotion, that is, by increasing the likelihood that a radiation-induced cancer would develop. In that case the PC would have no bias (see Chapter IV-G). Conceivably, other interaction models might also apply, which would affect bias differently.

Example 1 (Breast Cancer):

A woman diagnosed with a breast cancer at age 45, 19.7 years after an X-ray exposure at age 25 that delivered 10 rad to breast tissue.

$$F(D) = F(10) = 10$$

$$T(Y) = T(19) = 1$$

$$K(A_1,S) = K(25,f) = .00329 \text{ (Table X-10)}$$

$$R = F \times T \times K = 10 \times 1 \times .00329 = .0329$$

$$PC = R/(1+R) = .0329/1.0329 = .0319 = 3\%.$$

*   *   *

Example 2 (Bone Cancer):

A man diagnosed with bone cancer at age 20, 5.4 years after an exposure of 70 rad dose to the endosteal layer from alpha particle radiation at age 15.

$$F(D) = F(70) = 70$$

$$T(Y) = T(5) = .0814 \text{ (Table X-2-A)}$$

$$E(A_1,S) = E(15,m) = 2.79 \text{ (Table X-2-B)}$$

$$I(A_2,S) = I(20,m) = 1.12 \text{ (Table X-2-C)}$$

$$K = E/I = 2.79/1.12 = 2.49$$

$$R = F \times T \times K = 70 \times .0814 \times 2.49 = 14.19$$

$$PC = R/(1+R) = 14.19/15.19 = .934 = 93\%$$

$$*\quad*\quad*$$

The calculation of the relative excess where diagnosis occurred following several radiation exposures should be made by adding the relative excesses for each exposure. If doses $D(1)$, $D(2)$, and $D(3)$ occurred at ages $A(1)$, $A(2)$, and $A(3)$, respectively, the relative excess for the combined exposures is given by

$$R = R(1) + R(2) + R(3).$$

The PC of all these exposures is

$$PC = R/(1+R).$$

The PC for any one of them (say the first), given the change in risk c sed by the others, is

$$PC(1) = R(1)/(1+R).$$

$$*\quad*\quad*$$

Example 3   (Thyroid Cancer):

A man diagnosed with thyroid cancer at age 25, following a 30-rad X ray exposure to the thyroid at age 17, 8.2 years previously. As an infant (age 0, 24.7 years prior to diagnosis of thyroid cancer) the man was successfully treated by high-voltage X radiation for Wilms' tumor and it is estimated that his thyroid gland received 100 rad because of X-ray scatter. The PC for the combined exposures is calculated as follows:

For the first exposure, completely ignoring the second,

$$F(D) = F(100) = 100$$

$$T(Y) = T(24) = 1$$

$$K(A_1,S) = K(0,m) = .106 \text{ (Table X-12)}$$

$$R(1) = F \times T \times K = 100 \times 1 \times .106 = 10.6$$

For the second, ignoring the first,

$$F(D) = F(30) = 30$$

$$T(Y) = T(8) = .741$$

$$K(A,S) = K(17,m) = .0397 \text{ (Table X-12)}$$

$$R(2) = F \times T \times K = 30 \times .741 \times .0397 = .883$$

The relative excess R and the PC for the combined exposures are

$$R = R(1) + R(2) = 10.6 + .883 = 11.5$$

$$PC = R/(1 + R) = 11.5 / 12.5 = .920 = 92\%$$

$$*\quad*\quad*$$

Wilms' tumor is nearly always fatal unless treated, and it is highly likely that in the preceding example the high-voltage X ray therapy saved the patient's life. Thus the calculation of greatest interest might well concern the extent to which the patient's cancer is attributable to his second exposure alone. Simply ignoring the first exposure gives $R = R(2)$ and

$$PC(2) = R(2)/(1 + R(2)) = .883/1.883 = 0.468 = 47\%.$$

This calculation treats the patient as if he were a member of the general population; it is clear, however, that he is not. The radiation that saved the subject's life from Wilms' tumor also, as a side effect, increased his chances of getting thyroid later in life. Therefore he is a member of a subpopulation with a baseline rate that is different from the general population. As a group, men given a 100-rad thyroid dose in infancy have a thyroid cancer risk, in the absence of other exposure, $1 + R(1)$ times as large as that of the general population. Therefore the relative excess, <u>in the context of that subpopulation</u>, is

$$R'(2) = R(2)/(1 + R(1)) = .883/11.6 = .0761.$$

The PC calculated from R'(2) is

$$PC'(2) = R'(2)/(1 + R'(2)) = .0761/1.0761 = .0707 = 7\%.$$

The Ad Hoc Working Group considers the last calculation the most appropriate in this case.

In Chapter IV-F the quantity W is introduced as the ratio of baseline rates in the general population and the subpopulation. In the above example $W = 1/(1 + R(1))$, and $R'(2) = R(2) \times W$. This method allows the computation of a PC for a member of a population having a baseline risk different from the general population by means of the formula

$$R = F \times T \times K \times W,$$

provided that the factors causing the subpopulation to have a baseline risk

different from that of the general population are additive in effect with respect to radiation exposure.

Example 4 (Lung Cancer):

A lung cancer has been diagnosed in a 55-year-old man who was exposed to gamma rays at age 28 resulting in a 40-rad dose to the bronchial area of the lungs. He is a lifelong nonsmoker. If the PC calculation were carried out without regard to smoking history, it would be as follows:

$$F(D) = F(40) = 40 + 40/116 = 53.8$$

$$T(Y) = T(27) = 1$$

$$K(A_1,S) = K(28,m) = .000619 \text{ (Table X-9-A)}$$

$$R = F \times T \times K = 53.8 \times 1 \times .000619 = .0333$$

$$PC = R/(1+R) = .0333/1.0333 = .0322 = 3\%.$$

From Table X-9-A, however, the lung cancer rate of male nonsmokers is smaller than that of the general population by a factor of 6.81, and it appears that smoking and radiation interact additively in the causation of lung cancer (see Chapter IV-H). Thus W = 6.81, and the revised relative excess is

$$R = F \times T \times K \times W = 53.8 \times 1 \times .000619 \times 6.81 = .206,$$

from which

$$PC = R/(1+R) = .206/1.206 = .171 = 17\%.$$

* * *

Age at exposure, age at diagnosis, and time from exposure to diagnosis are tabulated in annual increments. For multiple, fractionated, or protracted exposures taking place at a single year of age A_1 and corresponding to the same value of Y, the doses can be summed provided that a linear dose-response model is appropriate for each exposure. If the linear-quadratic model applies, however, doses should be given for discrete 24-hour periods and treated as pertaining to separate exposures. In practice, however, there is little purpose to subdivide accumulated doses of less than 5 rad.

Example 5 (Acute Leukemia):

An acute leukemia was diagnosed at age 44 in a woman following several exposures to low-LET radiation at various ages. The first, to one rad average bone-marrow dose, occurred at age 20, 24 years and 2 months before diagnosis (Y=24). The second, to 2 rad, occurred 4 months later, at the same age (A=20) but 23 years and 10 months before diagnosis (Y=23). At age 21, 23 years and 3 months before diagnosis, 9 rad total dose was received over a 36-hour period at the continuous rate of 250 millirad per hour. Finally, at age 35, three exposures, to 1.1, 0.6, and 0.7 rad,

respectively, were received on consecutive days, 9 years and 2 months prior to diagnosis.

The first, second, and third exposures should be considered separately, because exposures 1 and 2 correspond to different values of Y, and exposures 2 and 3 to different exposure ages. The 9-rad continuous exposure delivered over 36 hours should be treated as 2 exposures because it required more than one day, but less than two. The partition giving the maximum risk estimate assigns 3 rad to one 24-hour period and 6 rad to another. The three exposures at age 35 can be treated as one because they correspond to the same values of A_1 and Y, and because the total dose is less than 5 rad.

Exposure 1:

$$F(D) = F(1) = 1 + 1^2/116 = 1.01$$

$$T(A_1,Y) = T(20,24) = .0101 \text{ (Table X-1-D)}$$

$$E(A_1,S) = E(20,f) = .914 \text{ (Table X-1-E)}$$

$$I(A_2,S) = I(44,f) = 2.73 \text{ (Table X-1-F)}$$

$$K = E/I = .914/2.73 = 0.335$$

$$R_1 = F \times T \times K = 1.01 \times .0101 \times .335 = .00342.$$

Exposure 2:

$$F(2) = 2 + 2^2/116 = 2.03$$

$$T(20,23) = .0114$$

$$E(20,f) = .914$$

$$I(44,f) = 2.73$$

$$K = E/I = .914/2.73 = 0.335$$

$$R_2 = F \times T \times K = 2.03 \times .0114 \times .335 = .00775$$

Exposure 3a:

$$F(3) = 3 + 3^2/116 = 3.08$$

$$T(21,23) = .0120$$

$$E(21,f) = .912$$

$$I(44,f) = 2.73$$

$$K = E/I = .912/2.73 = 0.334$$

$$R_{3a} = F \times T \times K = 3.08 \times .0120 \times .334 = .0123$$

Exposure 3b:

$$F(6) = 6 + 6^2/116 = 6.31$$

$$T(21,23) = .0120$$

$$E(21,f) = .912$$

$$I(44,f) = 2.73$$

$$K = E/I = .912/2.73 = 0.334$$

$$R_{3b} = F \times T \times K = 6.31 \times .0120 \times .334 = .0253$$

Exposures 4, 5, and 6:

$$F(1.1 + 0.6 + 0.7) = F(2.4) = 2.4 + 2.4^2/116 = 2.45$$

$$T(35,9) = .0436$$

$$E(35,f) = 1.24$$

$$I(44,f) = 2.73$$

$$K = E/I = 1.24/2.73 = 0.454$$

$$R_{4,5,6} = F \times T \times K = 2.45 \times .0436 \times .454 = .0485$$

$$R = R_1 + R_2 + R_{3a} + R_{3b} + R_{4,5,6} = .00342 + .00775 + .0123 + .0253 + .0485 = .0973$$

$$PC = R/(1+R) = .0973/1.0973 = .0887 = 9\%.$$

$$* \quad * \quad *$$

CHAPTER X: THE CALCULATION OF PROBABILITIES OF CAUSATION FOR CANCERS

OF SPECIFIC TISSUES

1. <u>Leukemia</u> (204-207, except 204.1, in 8th International Classification of Diseases Adapted for Use in the United States [ICDA])

    The derivation of PC values, described in Chapters IV-VI and IX, is more complex for the leukemias than for the solid tumors. The leukemogenic effect of ionizing radiation does not extend to all forms of leukemia, chronic lymphocytic leukemia (CLL) being the notable exception and there being possibly others of lesser importance, such as hairy-cell leukemia. The major forms of leukemia known to be caused by radiation, the acute forms (AL) and chronic granulocytic leukemia (CGL), differ in the likelihood of their occurrence following exposure to radiation, in their dependence upon age at exposure, and in their distribution over time following exposure.

    The only series of radiation-induced leukemias that even approaches the size needed to describe the leukemogenic effect of radiation derives from the studies of A-bomb survivors (1), and for the present purpose it was necessary to analyze those data in greater depth than was required for the BEIR III report in which the risk coefficients for leukemia were derived from the same source. Other human data on radiation leukemogenesis are in reasonable agreement as to the general magnitude of the risk per rad, the role of age at exposure, and the distribution of the radiogenic excess over time (2-4). There is, however, a question as to the comparability of risk coefficients based on partial-body irradiation with those based on whole-body exposure. As a working hypothesis for radiation protection purposes it has generally been assumed that a dose to a portion of the marrow can be averaged over the entire marrow so that, e.g., a dose of 800 rad to 40 percent of the marrow would average 320 over the whole body. This hypothesis, while consistent with a linear dose response, clearly is inconsistent with a model incorporating terms that are quadratic or otherwise nonlinear in dose. For example, if partial-body doses are high enough to kill or otherwise render ineffective a significant number of cells, as seems to be the case, e.g., with X-ray therapy for cervical cancer (5), the hypothesis is surely invalid.

    The Working Group has employed the linear-quadratic dose-response function preferred by the BEIR committee for low-LET radiation, but the present tables for calculating PC values distinguish between acute forms and chronic granulocytic leukemia, while providing coefficients for all forms considered as a group but excluding CLL. The material for all forms except CLL may be used in those instances where the precise type cannot be established and for chronic leukemias other than CLL and CGL. The A-bomb survivor material on which the BEIR estimates were based reflects diagnoses that generally were the latest and most definitive obtainable. Leukemia that is neither acute nor chronic at initial diagnosis eventually becomes acute. Therefore, the acute leukemia coefficients

probably should be used for such cases in preference to the all-types coefficients in the PC calculation. Death certificates may not specify histologic type, but are generally reliable for leukemia. The present report also differs from the BEIR report in its use of a "wave" function to distribute the radiogenic leukemia over time, the BEIR report having employed a plateau.

Data from the A-bomb survivor series (1) and the British ankylosing spondylitis series (3) were used to derive lognormal time-to-response models (see Chapter V-C). Time from exposure to response was assumed to be log-normally distributed with a two-year minimum. For chronic granulocytic leukemia (CGL) the fitted distribution of log(time in years − 2) was independent of age at exposure and sex, with mean 2.68 and variance 1.51, while for acute leukemia the variance was 0.65 and the mean $1.61 + .015A_1 + .0005A_1{}^2$, where A_1 denotes age at exposure.

The age-specific linear-quadratic risk coefficients in the BEIR III report for all types of leukemia except chronic lymphocytic leukemia (CLL) in fact pertained to only AL plus CGL. These were made specific to AL and CGL in the ratio 68:32, based on a reanalysis of the A-bomb survivor data (1). Coefficients for single years of age at exposure were derived by the procedure described in Chapter V-D.

Several studies (6,7) have reported excess childhood leukemias follow-ing fetal irradiation. Given the well-established association of leukemia with childhood exposure, the causality is less in doubt than the magnitude of the effect. The Working Group has made no distinction between fetal exposure and exposure during the first year of life.

The SEER data on the incidence of leukemia for the period 1973-1981 have been used as the source of age-, sex-, and type-specific incidence of leukemia in the general United States population (see Chapter VII-C). The ICDA-8 code equivalents used were:

chronic granulocytic − 205.1

acute − 204.0, 204.9, 205.0, 205.9, 206.0

206.9, 207.0, 207.2, 207.9

all except CLL − 204.0. 204.9, 205.1, 205.9, 206.0,

206.1, 206.9, 207.0, 207.2, 207.9

The reporting areas for the SEER program (8) are relatively homogeneous as to their incidence of leukemia (see Tables VII-1, and VII-2).

Although the leukemogenic potential of a variety of chemicals is much discussed, it is only for benzene that reasonably cogent evidence is in hand (9). Thus, it is not often that risk factors other than radiation will be identified and appear to compete with radiation. The influence of risk factors other than ionizing radiation is discussed in Chapter IV, Sections E to G and in Chapter IX.

For leukemia, the relative excess, R, in the basic equation

$$PC = R/(1 + R)$$

is found as the product of three functions, i.e.,

$$R = F(D) \times T(A_1,Y) \times K(A_1,A_2,S)$$

where D is the tissue dose in rad for low-LET radiation; $T(A_1,Y)$ represents the conditioning influence of age at exposure A_1 and time to diagnosis (Y); and $K(A_1,A_2,S)$ represents the relative excess of leukemia for a person of sex S, age at exposure A_1, and age at diagnosis A_2, when both F and T = 1. The standardized relative excess $K = K(A_1,A_2,S)$ for an exposure at age A_1 and diagnosis at age A_2 is the ratio of the estimated lifetime absolute excess $E = E(A_1,S)$ and the background incidence $I = I(A_2,S)$:

$$K(A_1,A_2,S) = E(A_1,S)/I(A_2,S).$$

The coefficient E was derived from the BEIR III coefficients, fitted to a quadratic function in age A_1 (see Chapter V-D), and is an estimate of the probability that a radiation-induced leukemia of the specified type will be diagnosed at some time after exposure given F(D) = 1. For each exposure age A_1 and sex S, $E(A_1,S)$ was determined such that the average of $E(A_1,S) \times T(A_1,Y)$ over the period Y = 2 through 28 was equal to the interpolated BEIR coefficient for age A_1 and sex S.

The following look-up tables are provided below:

      for CGL: T(Y), Table X-1-A;

               $E(A_1,S)$, Table X-1-B;

               $I(A_1,S)$, Table X-1-C;

    for all acute forms of leukemia: $T(A_1,Y)$, Table X-1-D;

                                    $E(A_1,S)$, Table X-1-E;

                                    $I(A_2,S)$, Table X-1-F;

    for all forms of leukemia except CLL: $T(A_1,Y)$, Table X-1-G;

                                          $E(A_1,S)$, Table X-1-H;

                                          $I(A_2,S)$, Table X-1-I.

Under the linear-quadratic model assumed for leukemia when exposure is to low-LET radiation, and the dose, D, is expressed in rad,

$$F = D + D^2/116.$$

The constant relative risk model for time to response does not hold for leukemia, which appears to follow a "wave" function. The factor T is the probability that a cancer caused by an exposure to radiation at age A_1 will be diagnosed Y years later. T depends only on Y for CGL, but on both Y and A_1 for AL and for all types considered as a group.

Several examples are provided to illustrate the procedures for calculating individual PC values:

Example #1   A typical female aged 5 at exposure to 5 rad of low-LET radiation to the bone marrow, with a diagnosis of acute leukemia at age 9, 4.2 years after exposure. Here, $D = 5$, $A_1 = 5$, $A_2 = 9$, and $Y = 4$.

$$F(D) = 5 + 5^2/116 = 5.22;$$

$$T(A_1,Y) = T(5,4) = .122, \text{ Table X-1-D};$$

$$E(A_1,S) = E(5,f) = 2.04, \text{ Table X-1-E};$$

$$I(A_2,S) = I(9,f) = 2.22, \text{ Table X-1-F};$$

$$K(A_1,A_2,S) = K(5,9,f) = E/I = 2.04/2.22 = .919;$$

then $R = F \times T \times K = 5.22 \times .122 \times .919 = .585;$

and, finally, $PC = R/(1 + R) = .369$ or 37%.

Example #2   A typical female, exposed at age 45 to 5 rad of low-LET radiation to the marrow, with a diagnosis of leukemia at age 53, 8 years after exposure, the leukemia not being well-established as to chronicity. In this case, one would use the acute leukemia tables: $D = 5$, $A_1 = 45$, $A_2 = 53$, and $Y = 8$;

$$F(D) = 5 + 5^2/116 = 5.22;$$

$$T(A_1) = T(45,8) = .0159, \text{ Table X-1-G};$$

$$E(A_1,S) = E(45,f) = 2.37, \text{ Table X-1-H};$$

$$I(A_1,S) = I(53,f) = 4.21, \text{ Table X-1-I};$$

and $K = E/I = 2.37/4.21 = .563$

then $R = F \times T \times K = 5.22 \times .0159 \times .563 = .0467$

and $PC = R/(1 + R) = .0446$ or 4%.

Example #3   A typical male, exposed at age 35 to 10 rad of low-LET radiation, with a diagnosis of CLL at age 60. In this case, no calculation would be made as CLL is not an eligible diagnosis.

The uncertainty surrounding PC estimates is discussed in Chapter VII, and Section VII-O includes a derivation of approximate 90 percent credibility intervals for PC estimates.

To provide a general orientation to the magnitude of the PC values that result from the procedures described here, Fig. X-1-A, B, and C have been prepared for CGL, acute forms, and all forms respectively. They give PC values for 1, 10, and 100 rad of low-LET radiation to the bone marrow by age at diagnosis, separately for males and females, and each has 8 parts corresponding to ages 0, 10, 20, 30, 40, 50, 60, and 70 at exposure. The vertical scale is logarithmic and curves are presented for only three radiation dose levels. For these and other reasons interpolation is to be discouraged.

Fig X-1-A-1

CHRONIC GRANULOCYTIC LEUKEMIA
EXPOSURE AGE 0
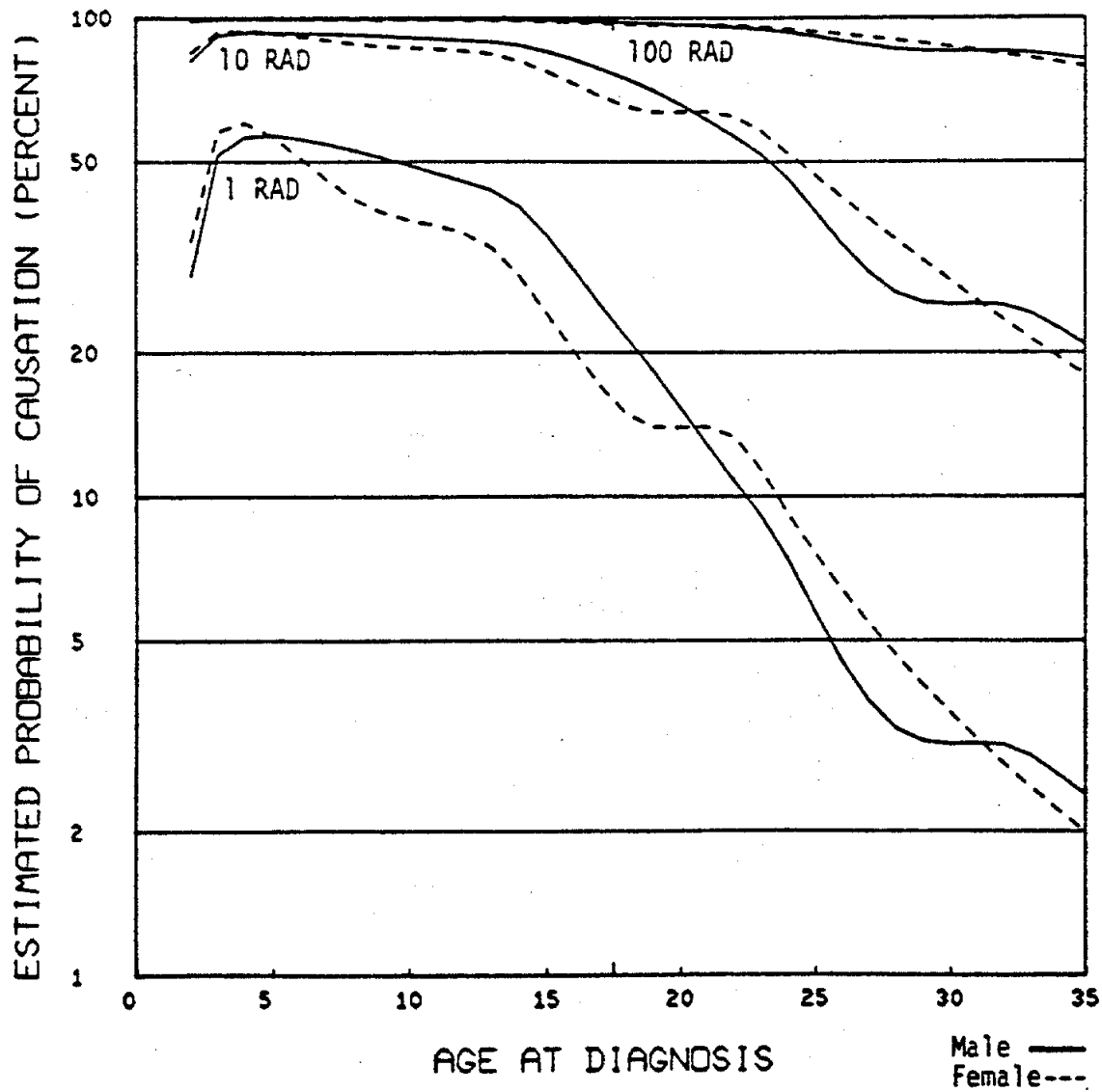
Fig X-1-A-2

CHRONIC GRANULOCYTIC LEUKEMIA
EXPOSURE AGE 10
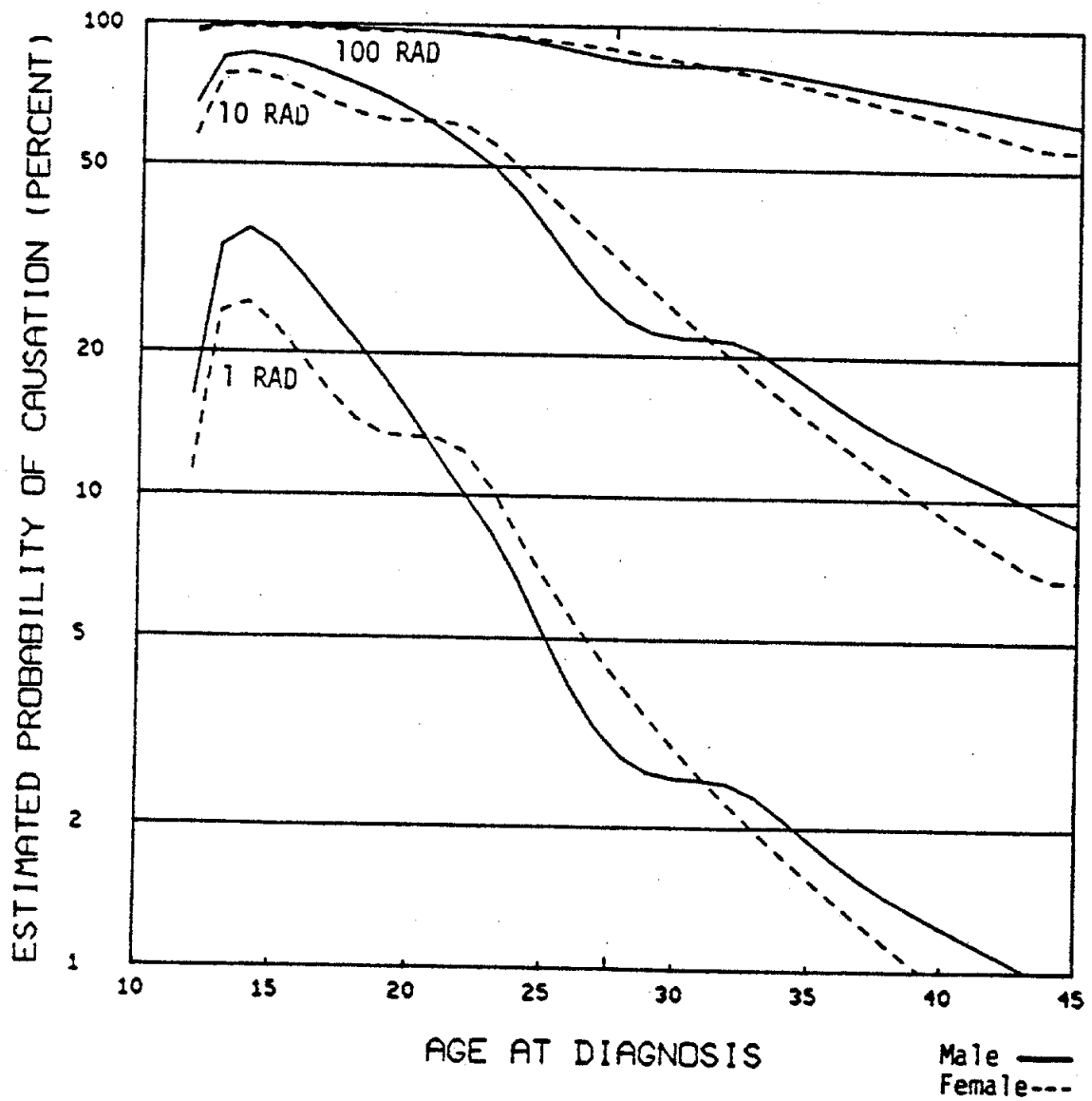
Fig X-1-A-3

CHRONIC GRANULOCYTIC LEUKEMIA
EXPOSURE AGE 20
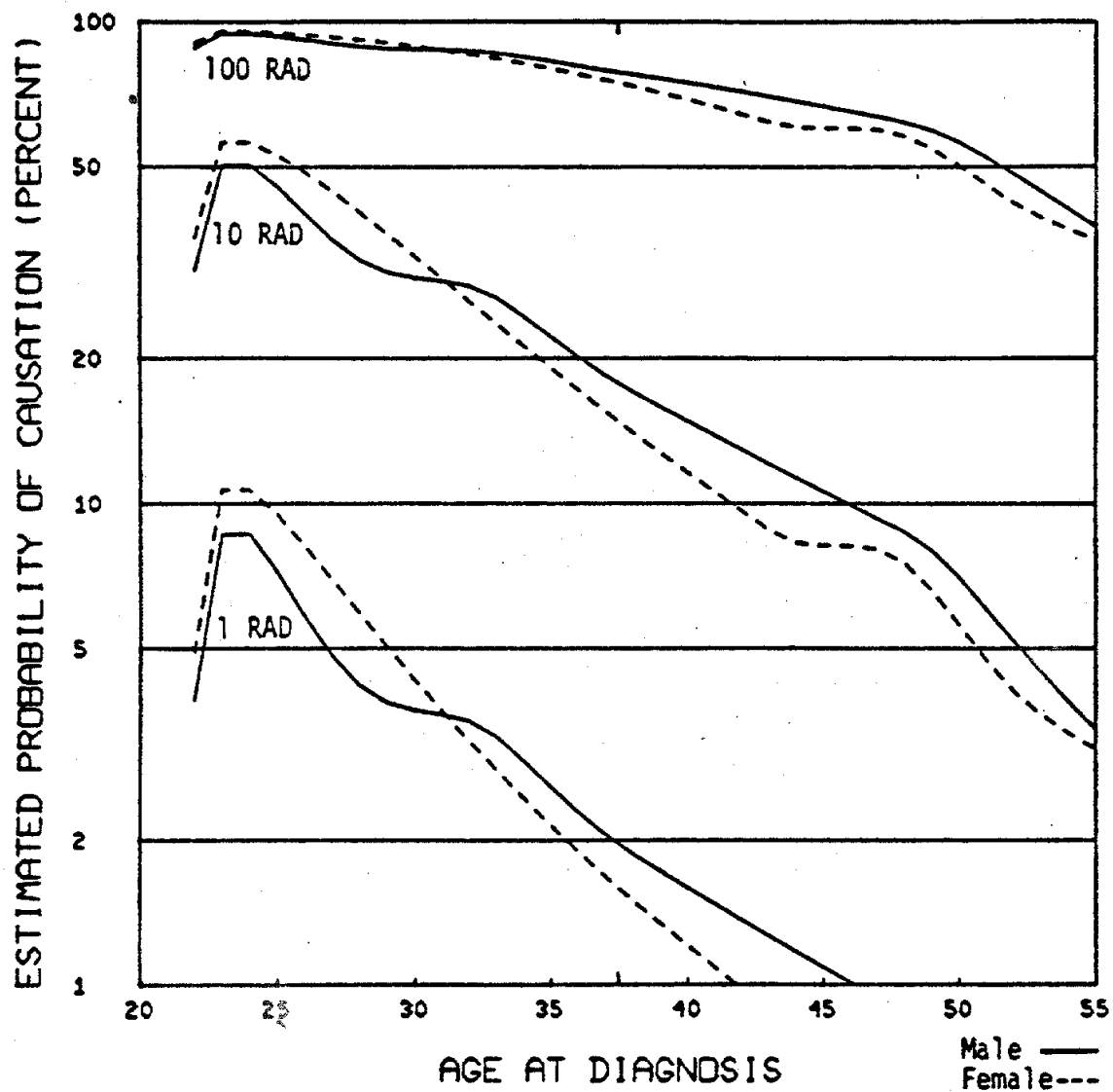
Fig X-1-A-4

CHRONIC GRANULOCYTIC LEUKEMIA
EXPOSURE AGE 30
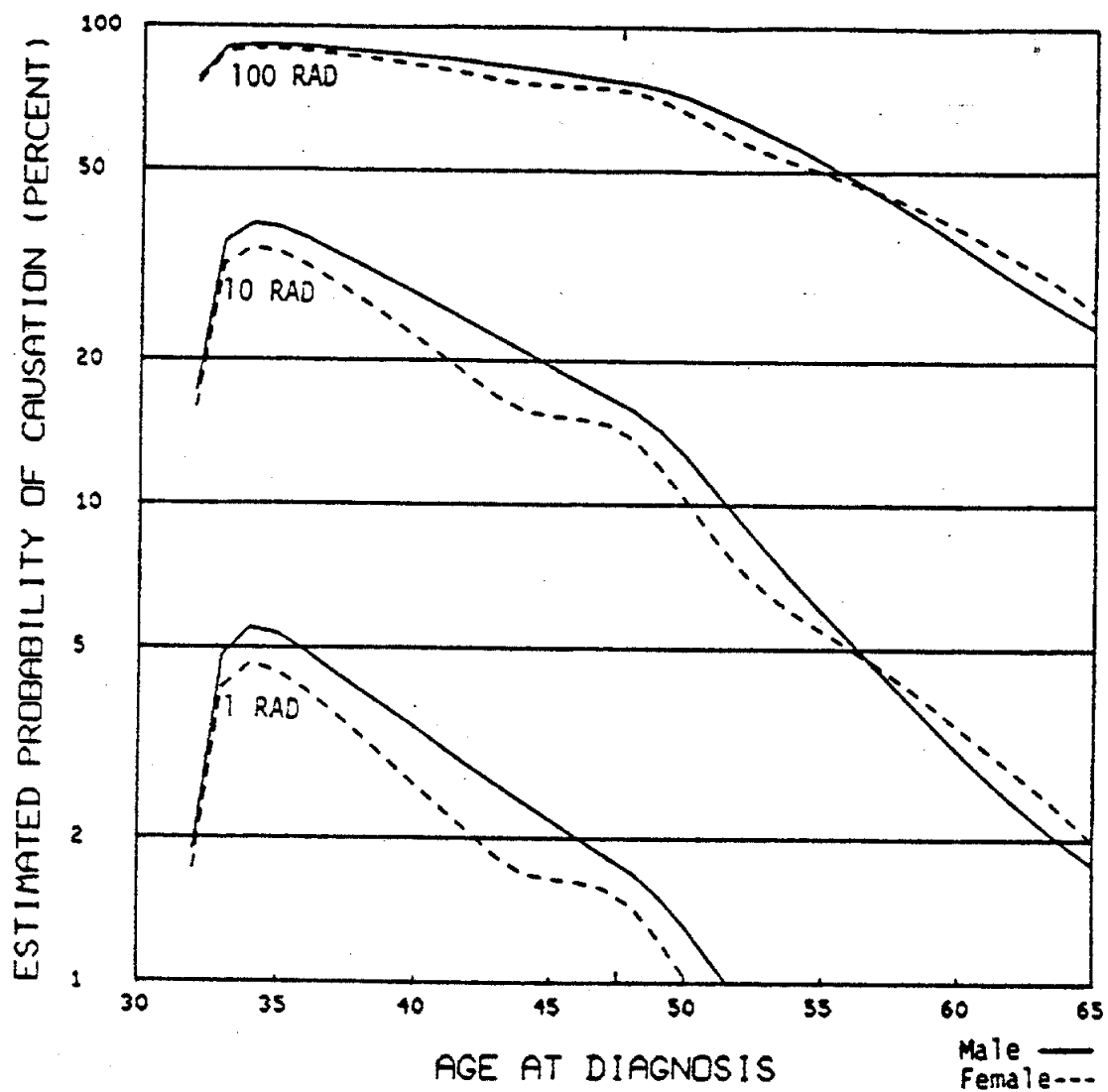
Fig X-1-A-5

CHRONIC GRANULOCYTIC LEUKEMIA
EXPOSURE AGE 40
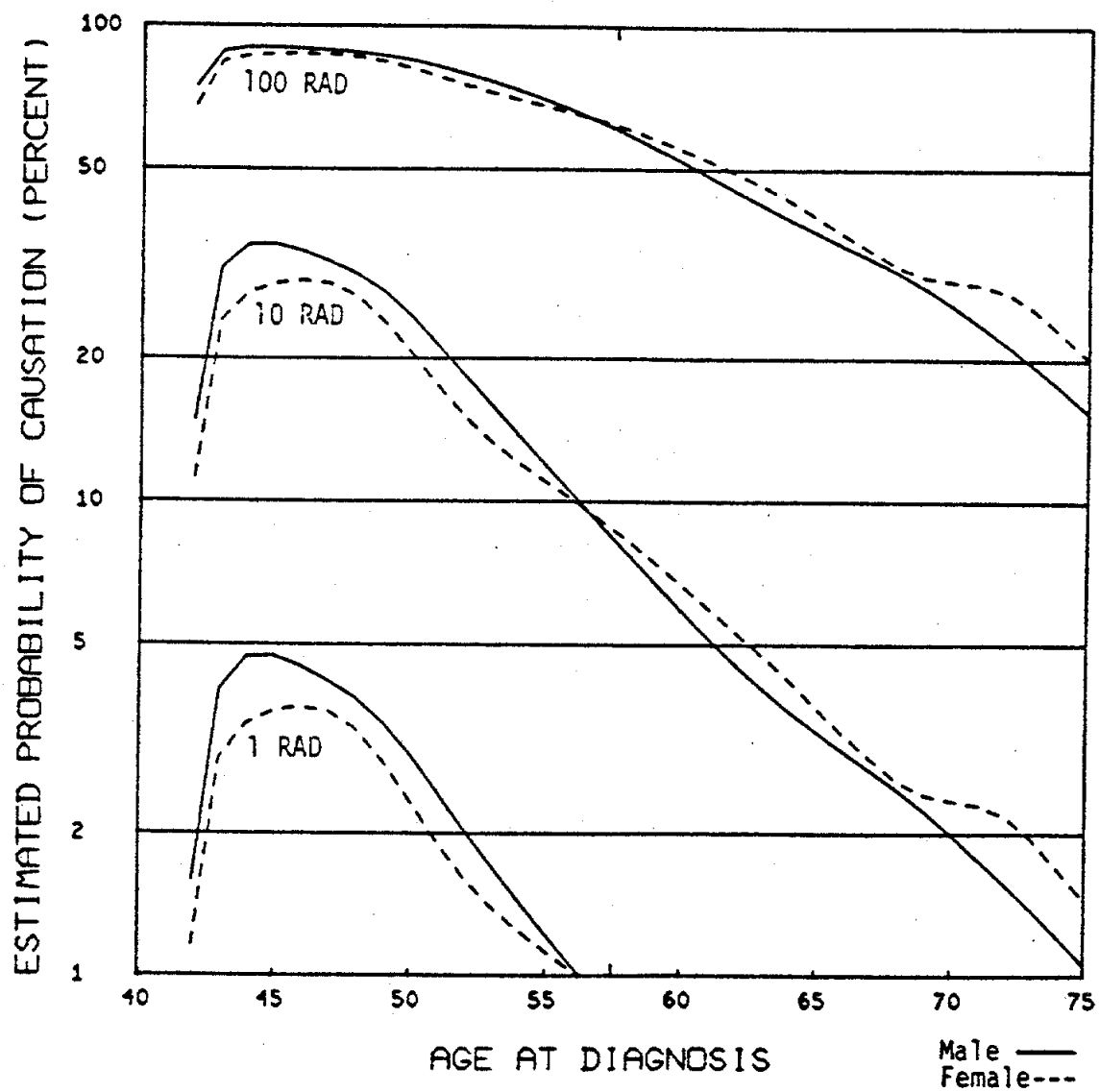
Fig X-1-A-6

CHRONIC GRANULOCYTIC LEUKEMIA
EXPOSURE AGE 50
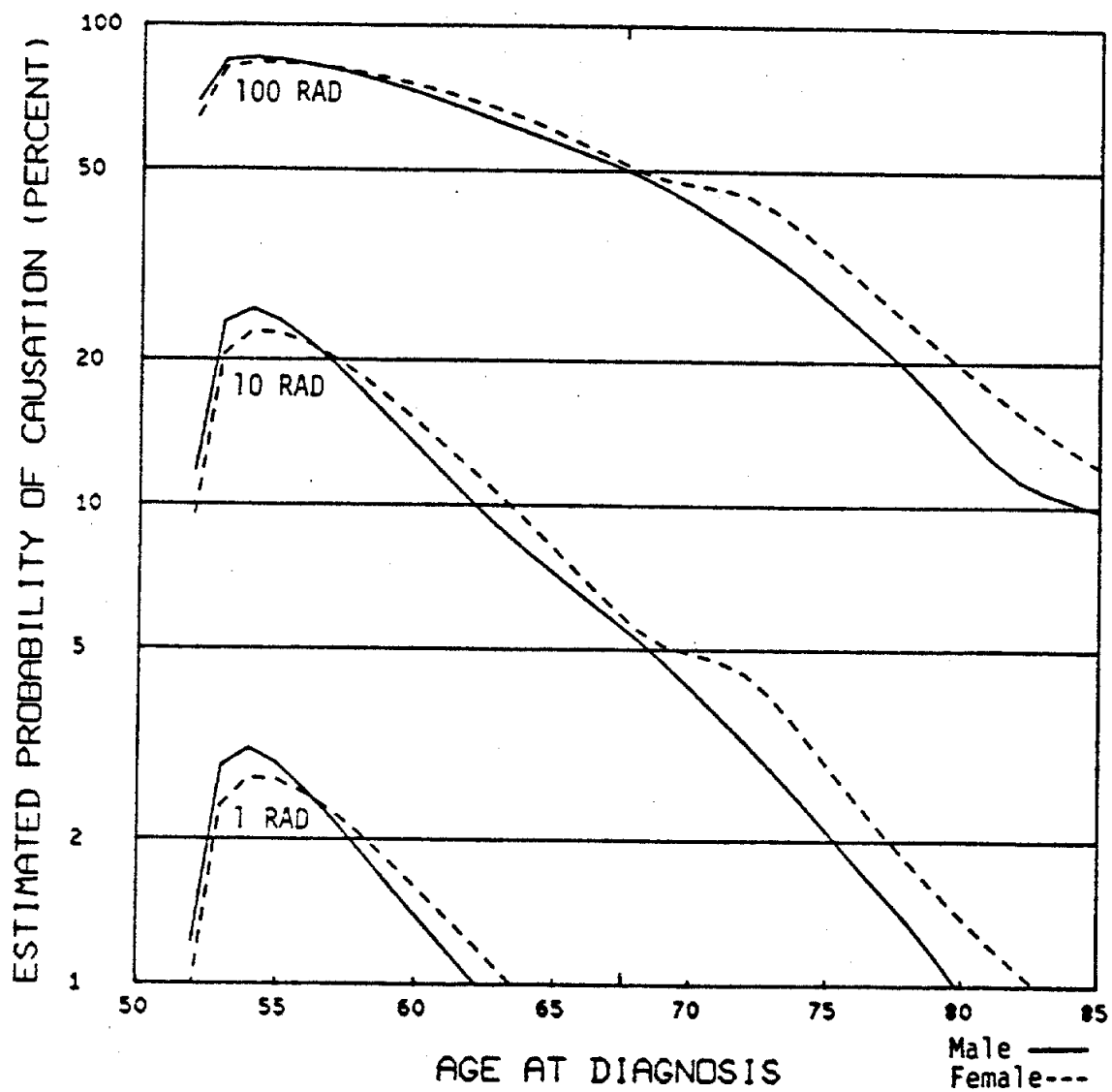
Fig X-1-A-7

CHRONIC GRANULOCYTIC LEUKEMIA
EXPOSURE AGE 60
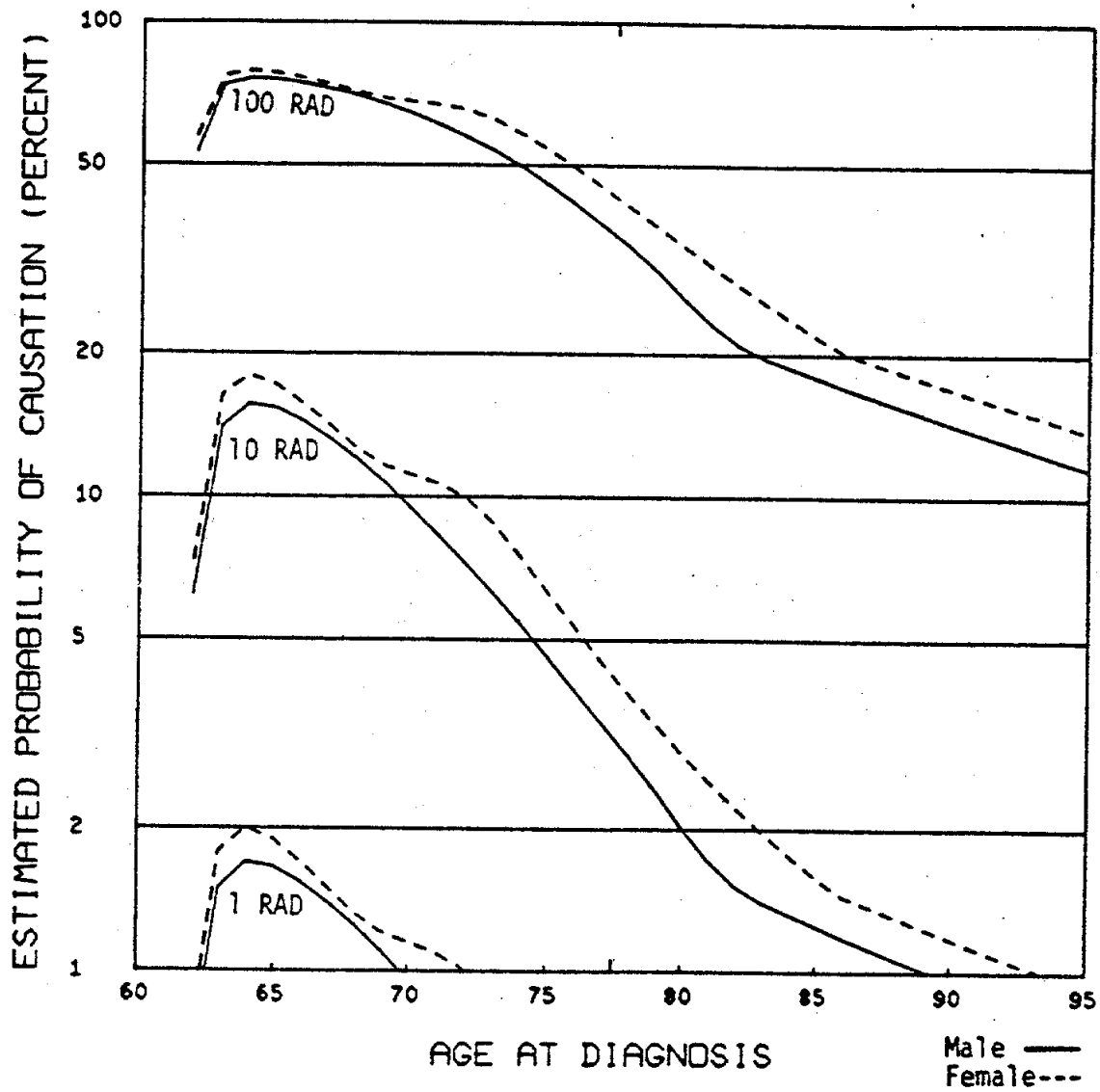
Fig X-1-A-8

CHRONIC GRANULOCYTIC LEUKEMIA
EXPOSURE AGE 70
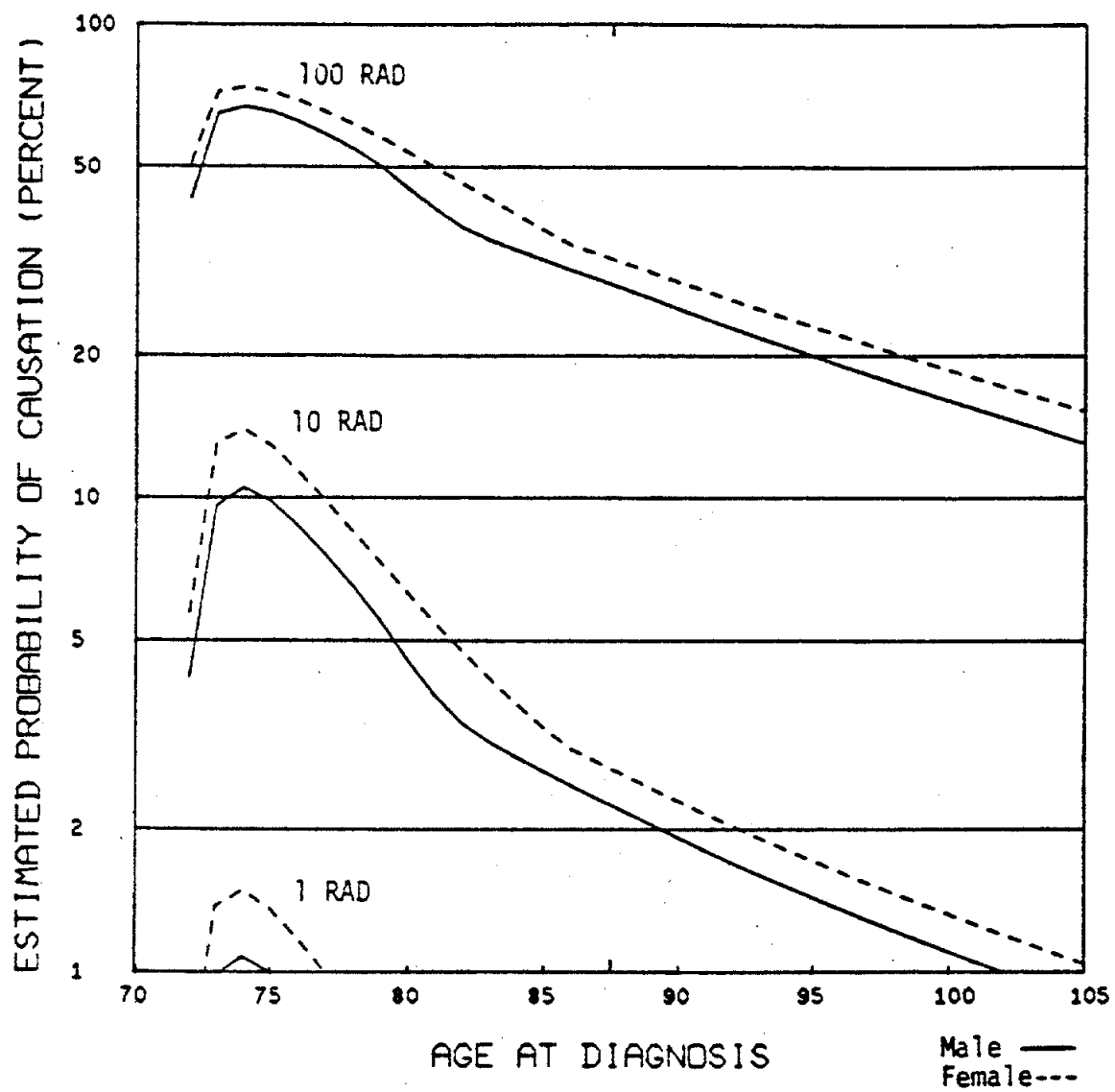
Fig X-1-B-1

ACUTE LEUKEMIA
EXPOSURE AGE 0
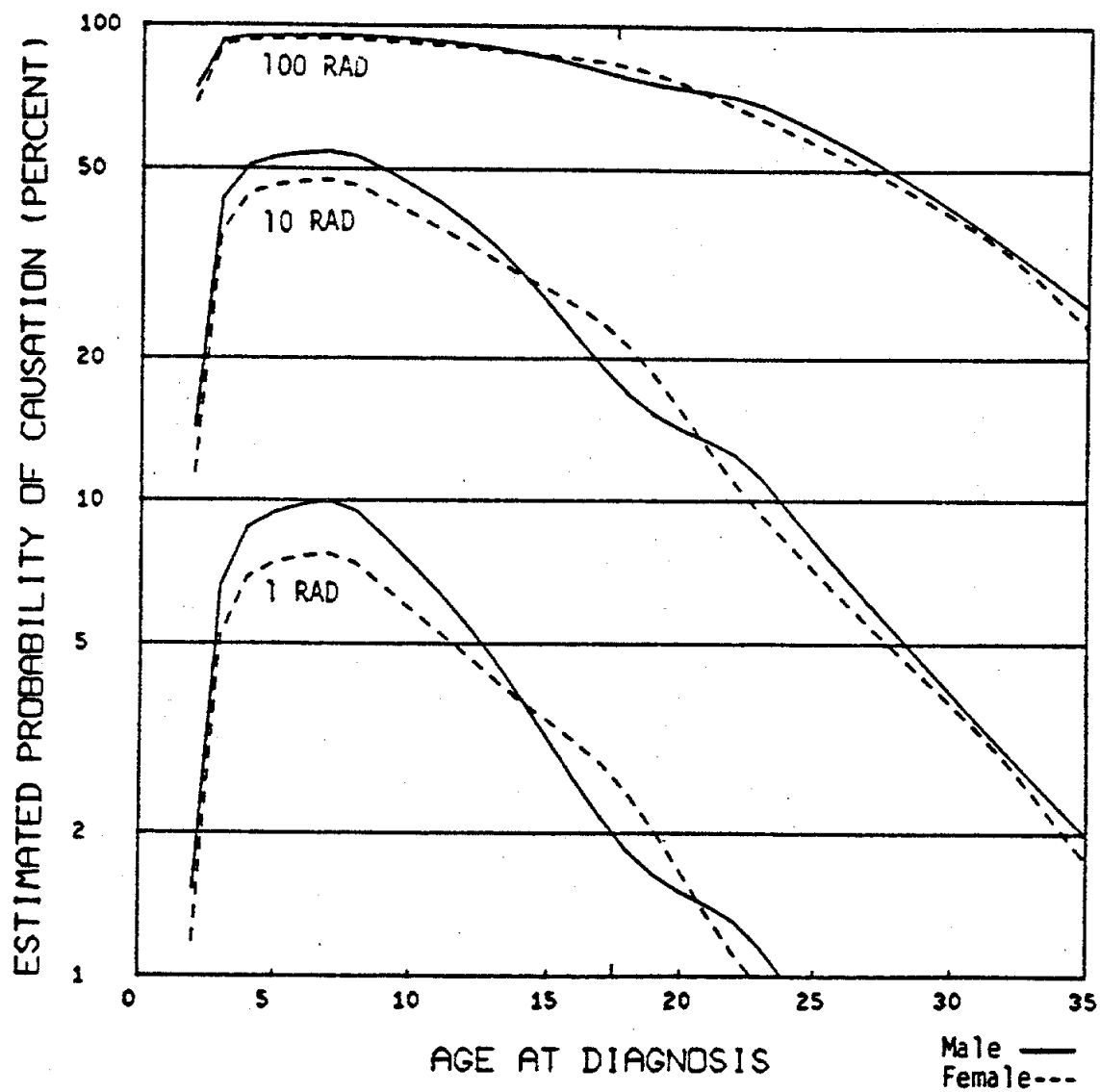
Fig X-1-B-2

ACUTE LEUKEMIA
EXPOSURE AGE 10
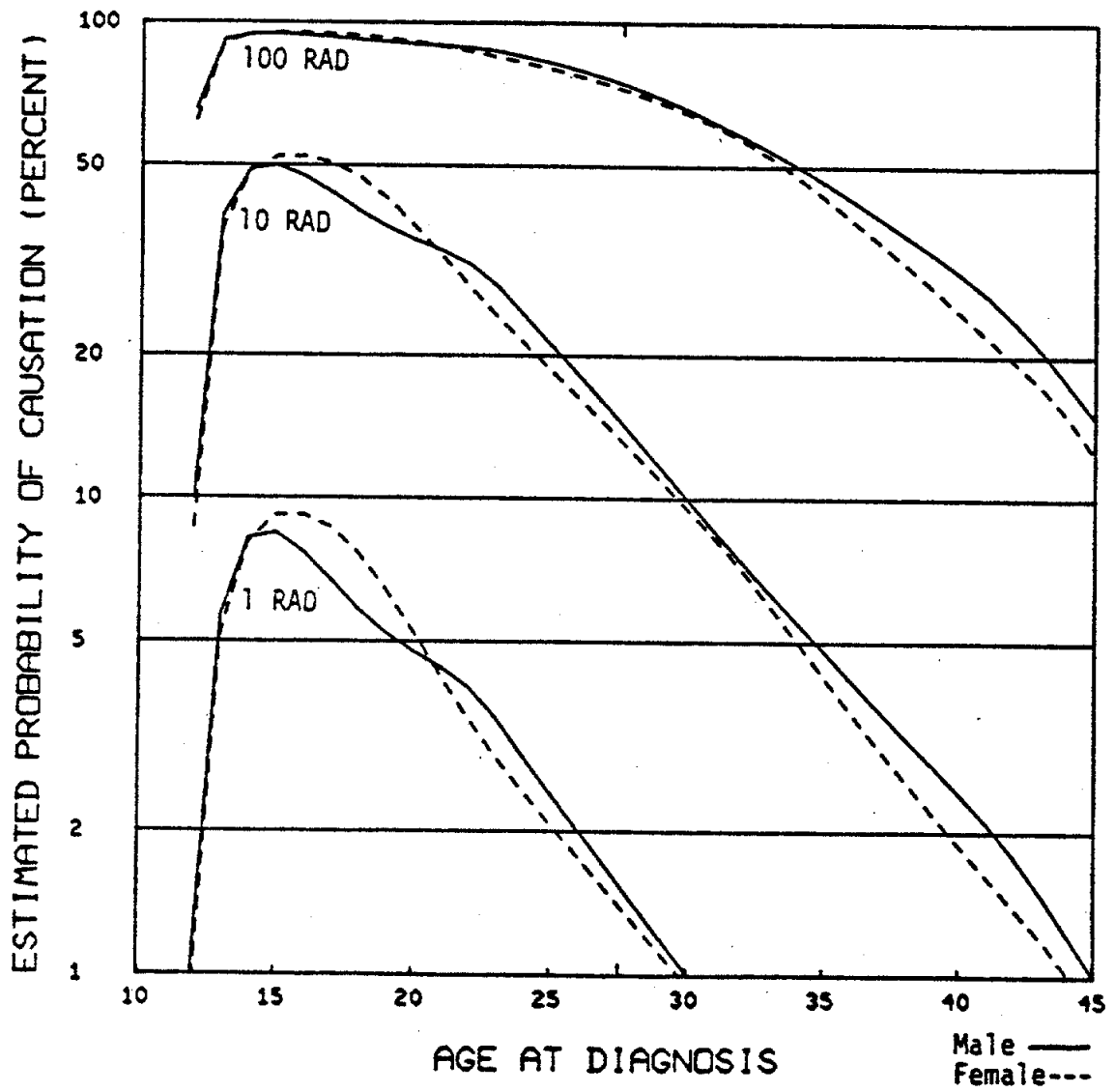
Fig X-1-B-3

ACUTE LEUKEMIA
EXPOSURE AGE 20
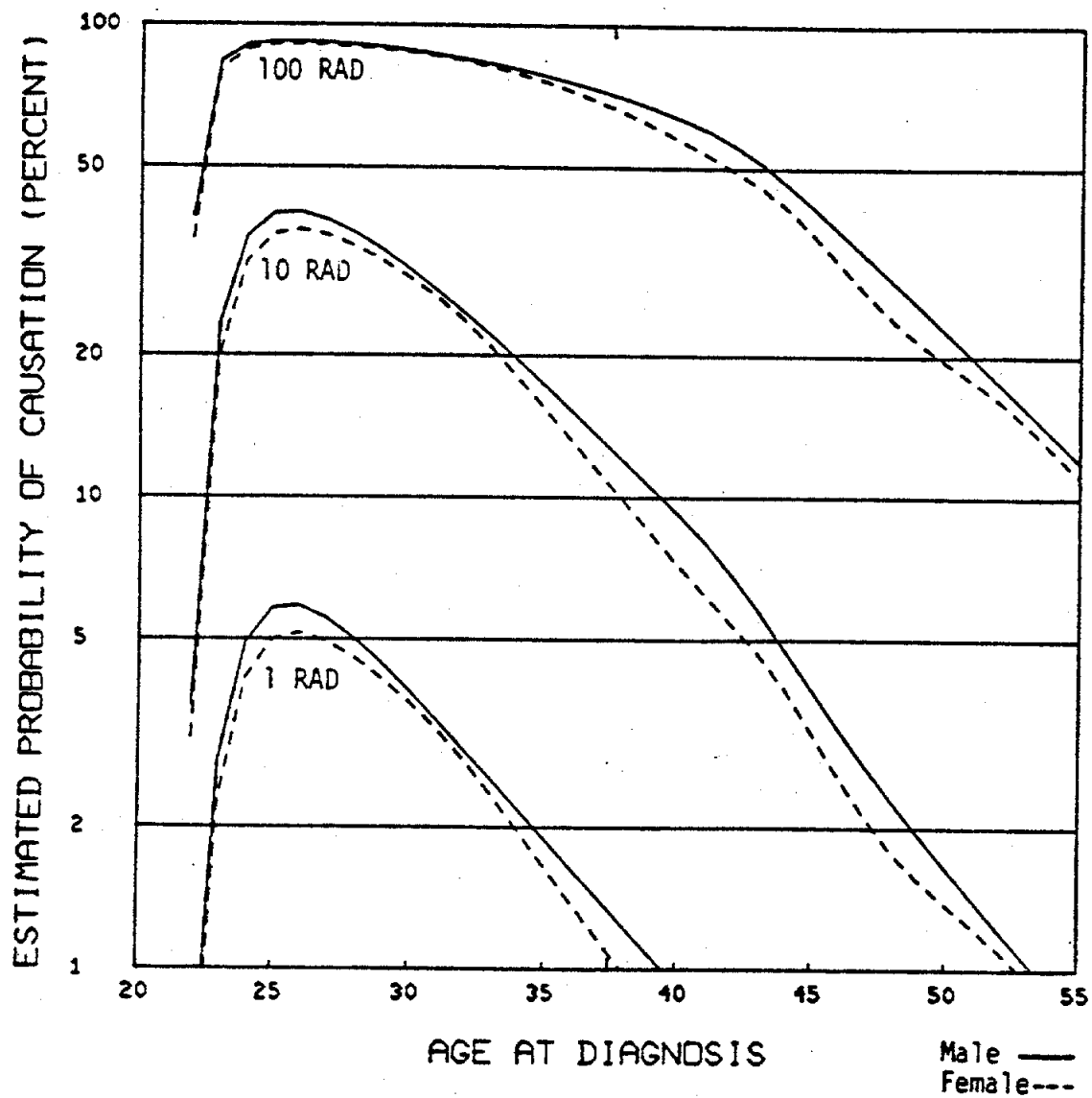
Fig X-1-B-4

ACUTE LEUKEMIA
EXPOSURE AGE 30
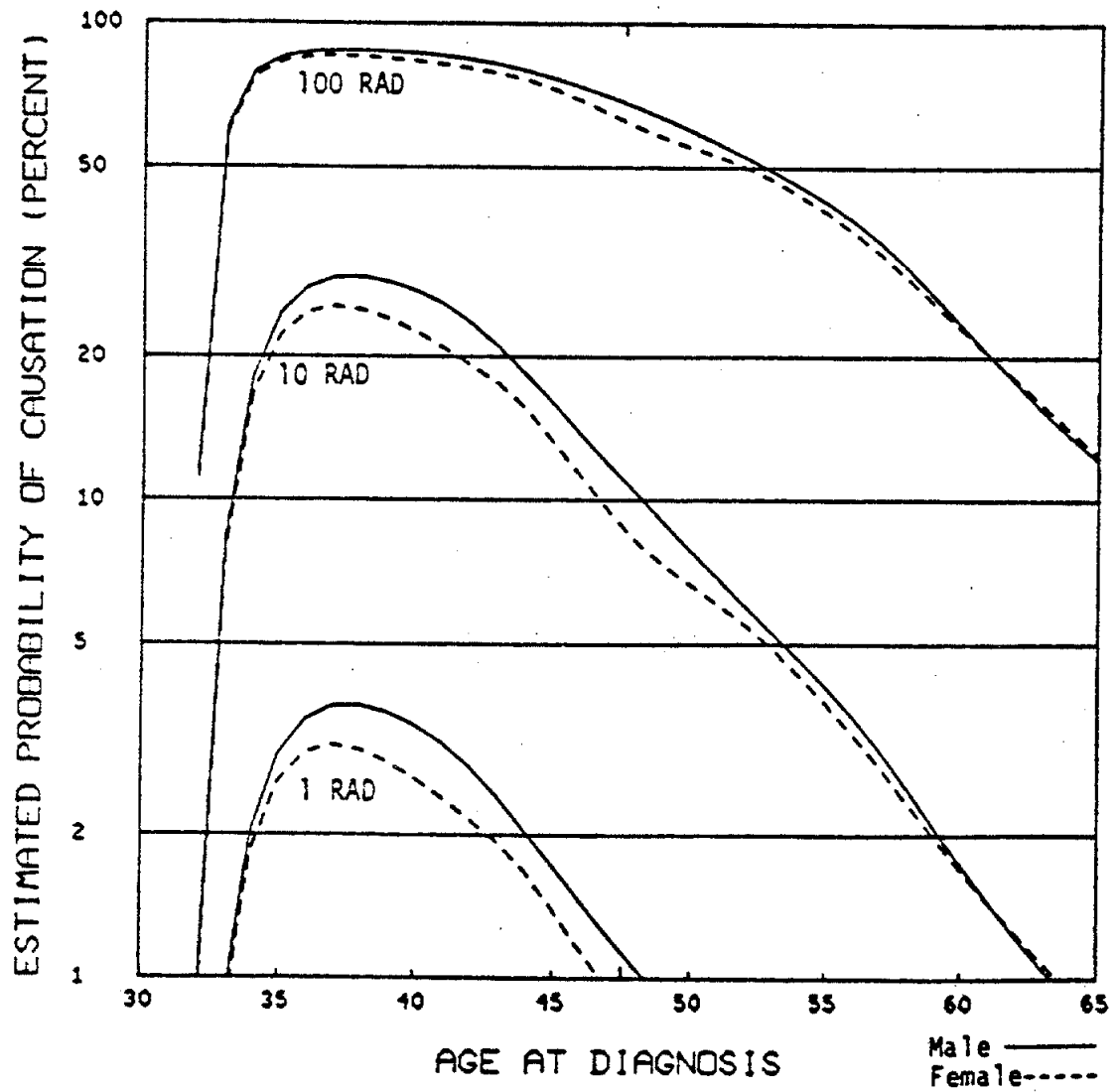
Fig X-1-B-5

ACUTE LEUKEMIA
EXPOSURE AGE 40
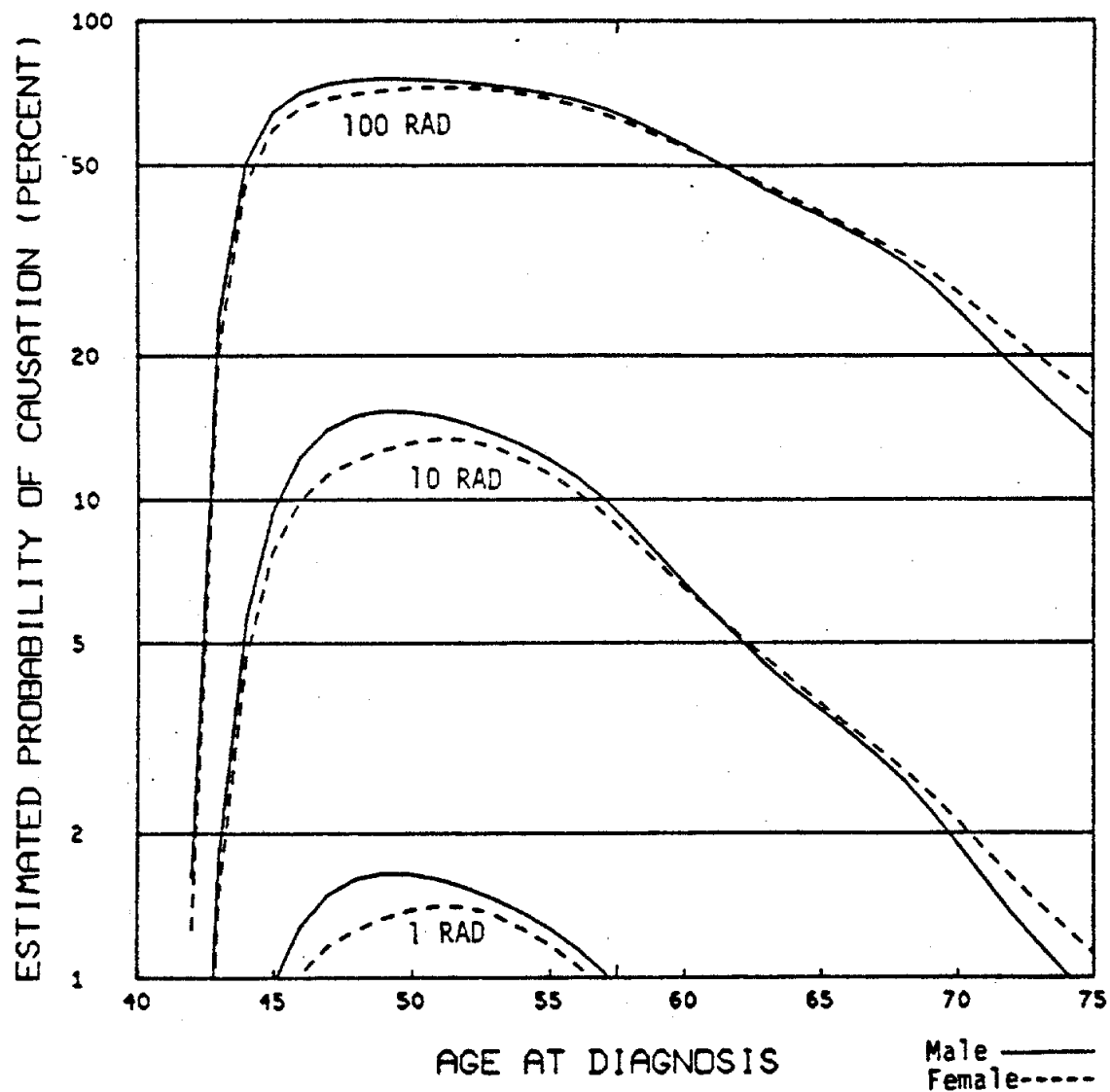
Fig X-1-B-6

ACUTE LEUKEMIA
EXPOSURE AGE 50
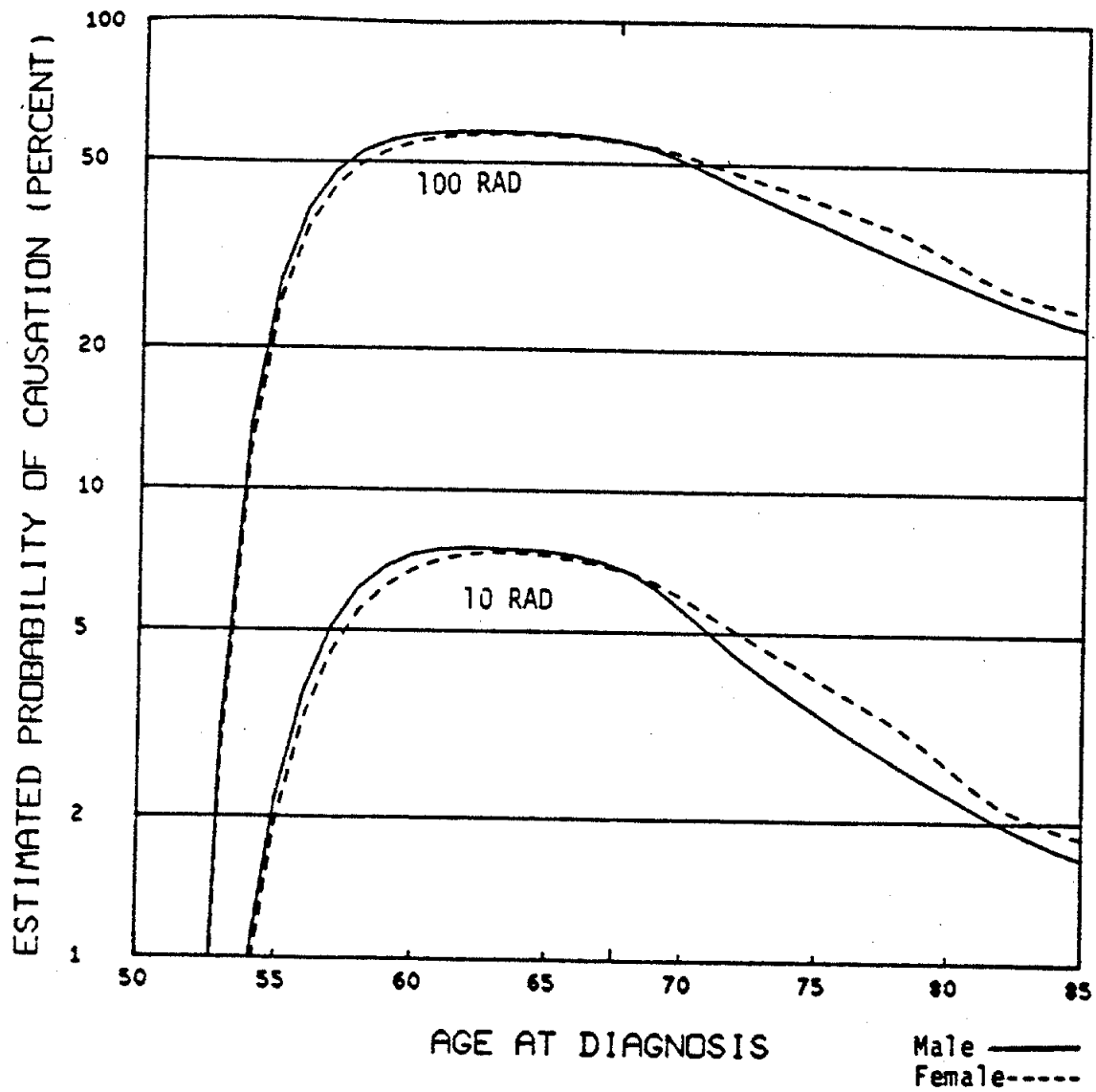
Fig X-1-B-7

ACUTE LEUKEMIA
EXPOSURE AGE 60

Fig X-1-B-8
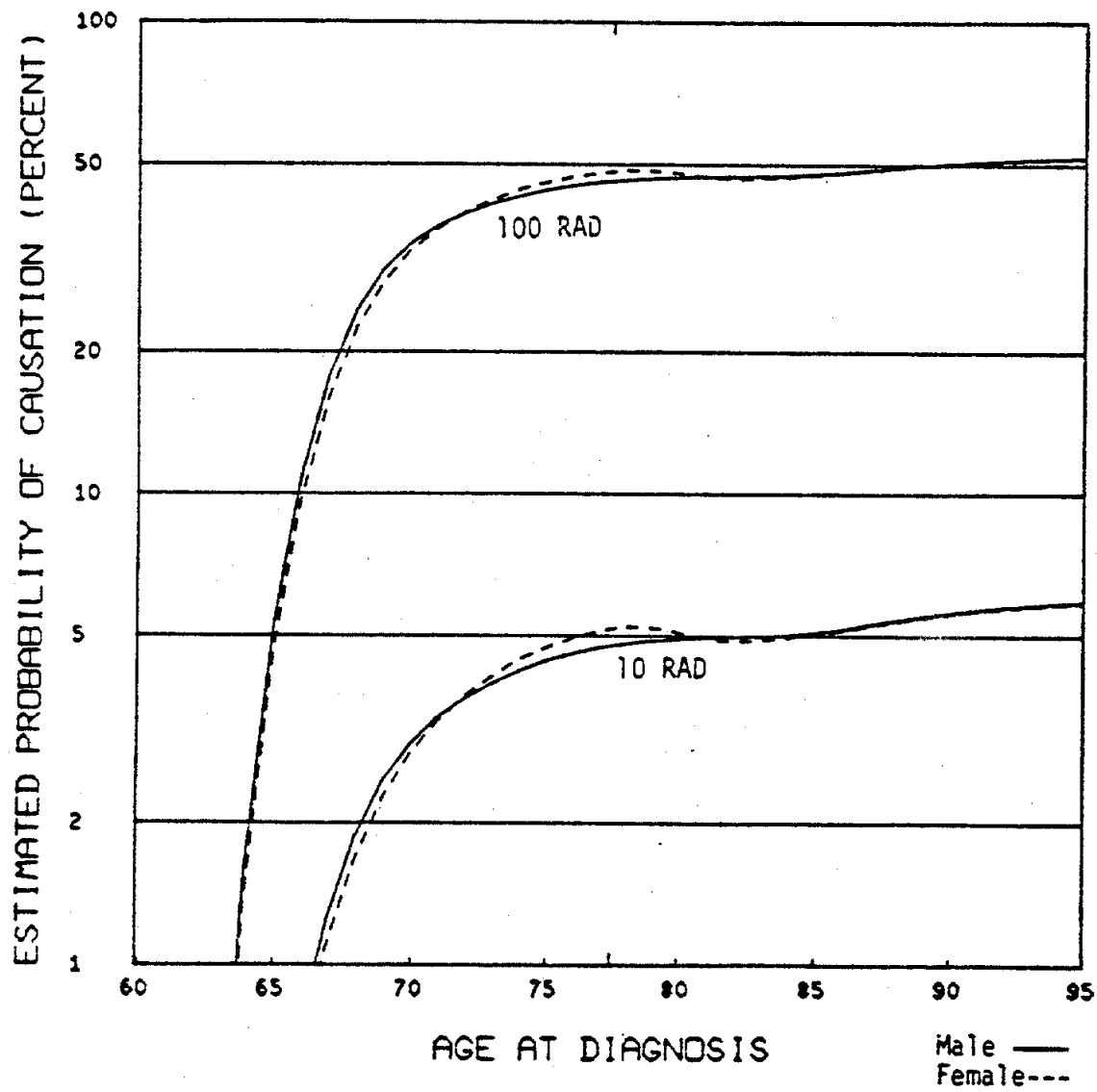
ACUTE LEUKEMIA
EXPOSURE AGE 70
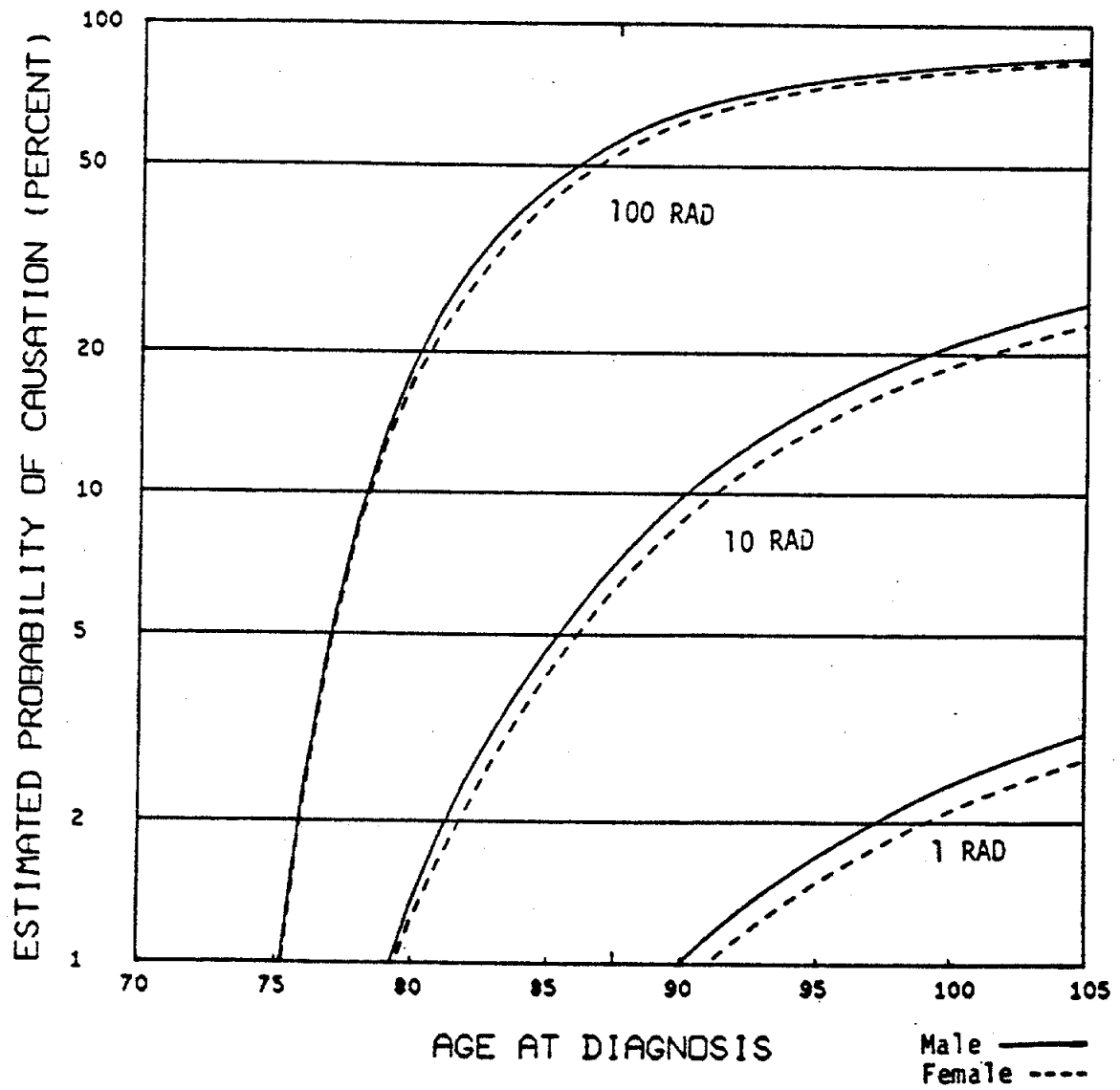
Fig X-1-C-1

LEUKEMIA: ALL TYPES EXCEPT CLL
EXPOSURE AGE 0
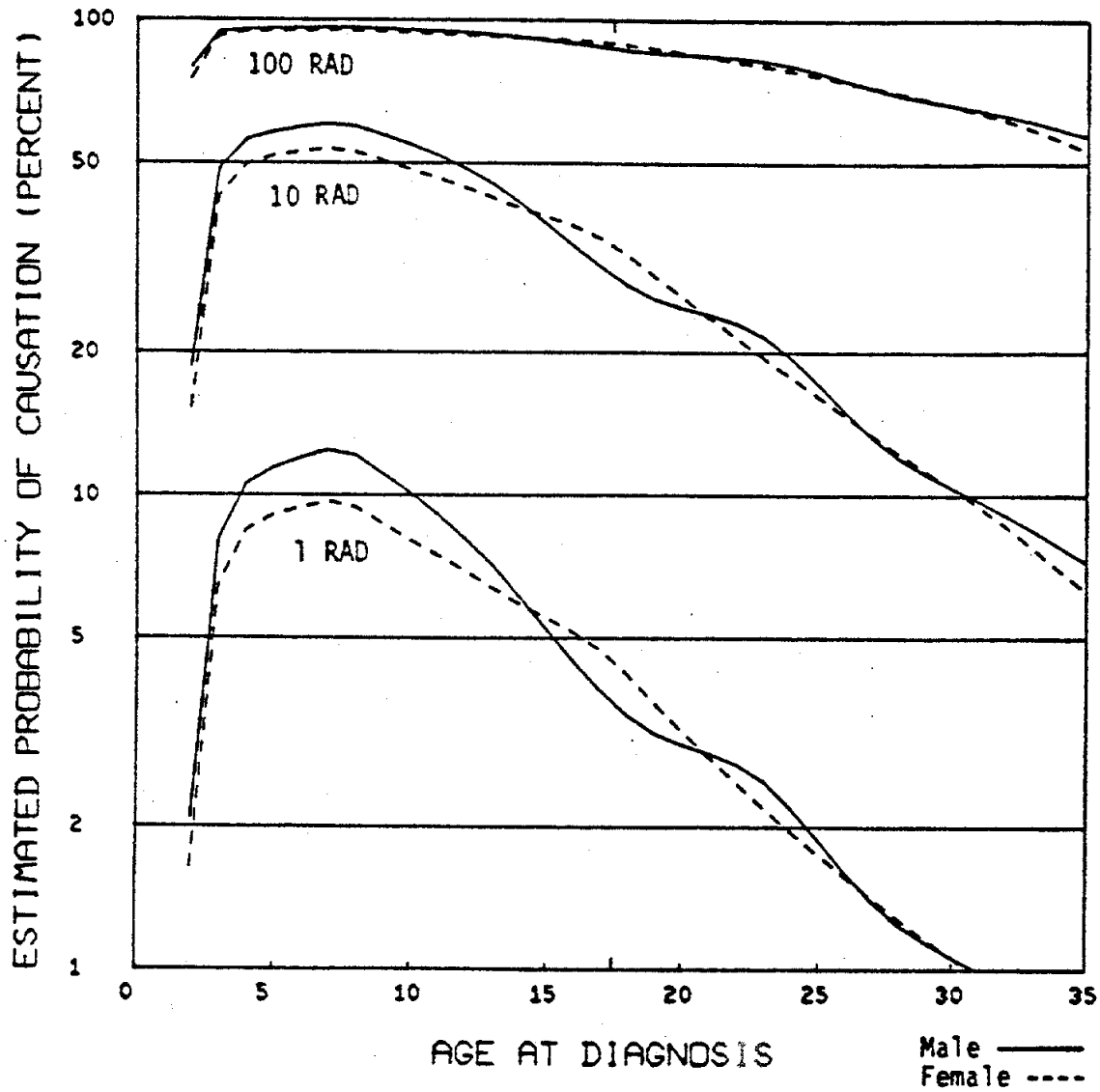
Fig X-1-C-2

LEUKEMIA: ALL TYPES EXCEPT CLL
EXPOSURE AGE 10
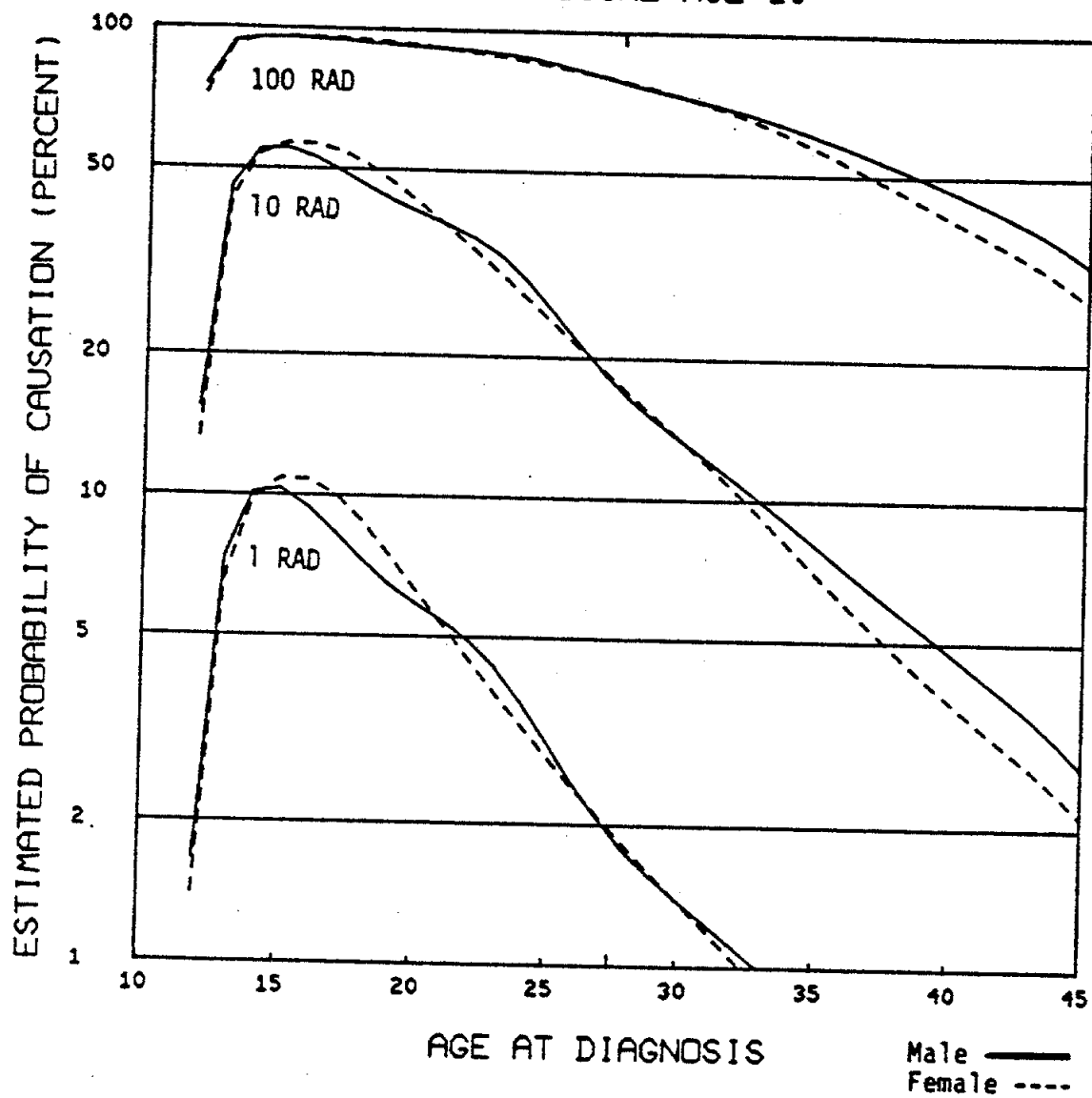
Fig X-1-C-3

LEUKEMIA: ALL TYPES EXCEPT CLL
EXPOSURE AGE 20
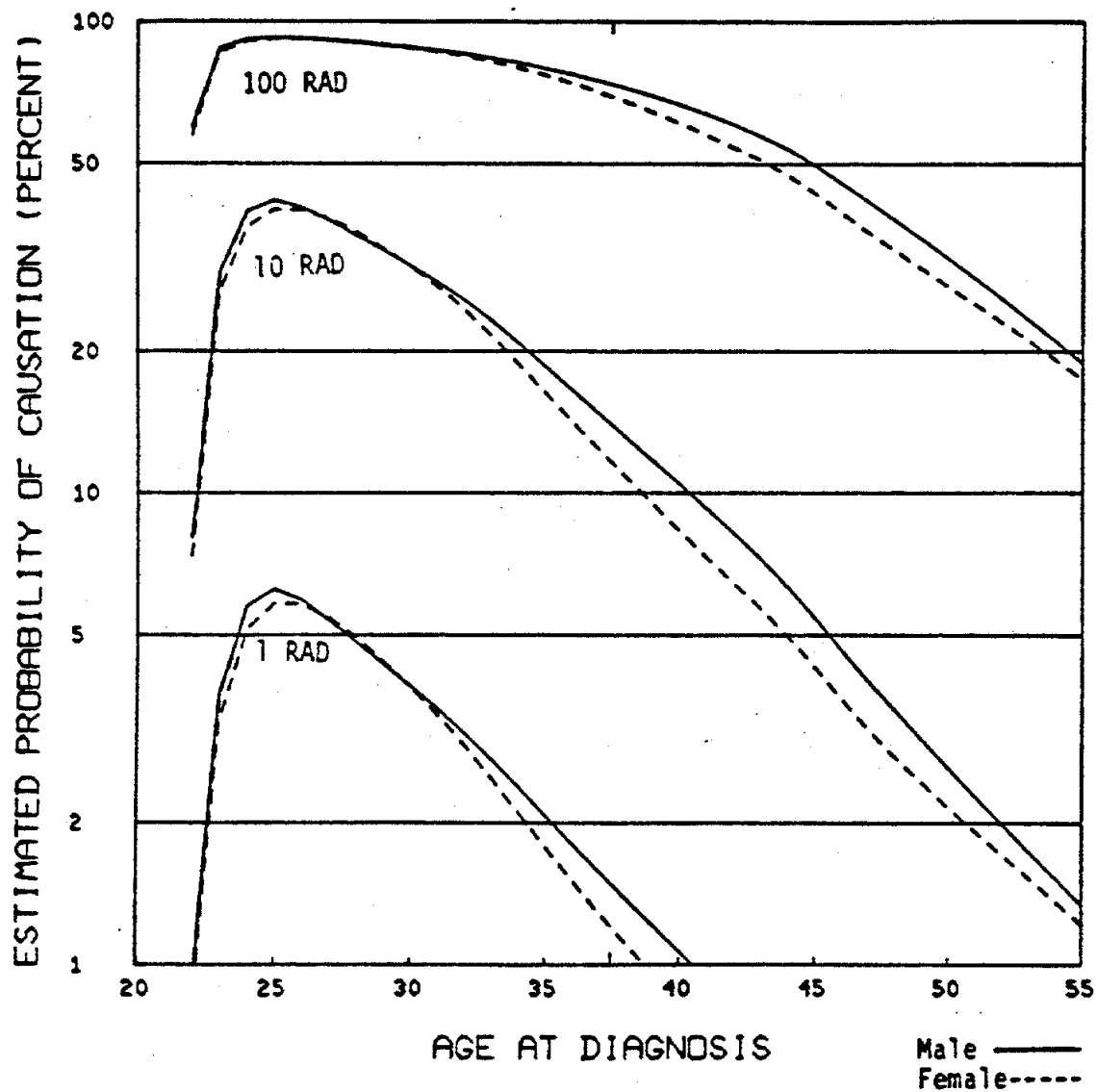
Fig X-1-C-4

LEUKEMIA: ALL TYPES EXCEPT CLL
EXPOSURE AGE 30
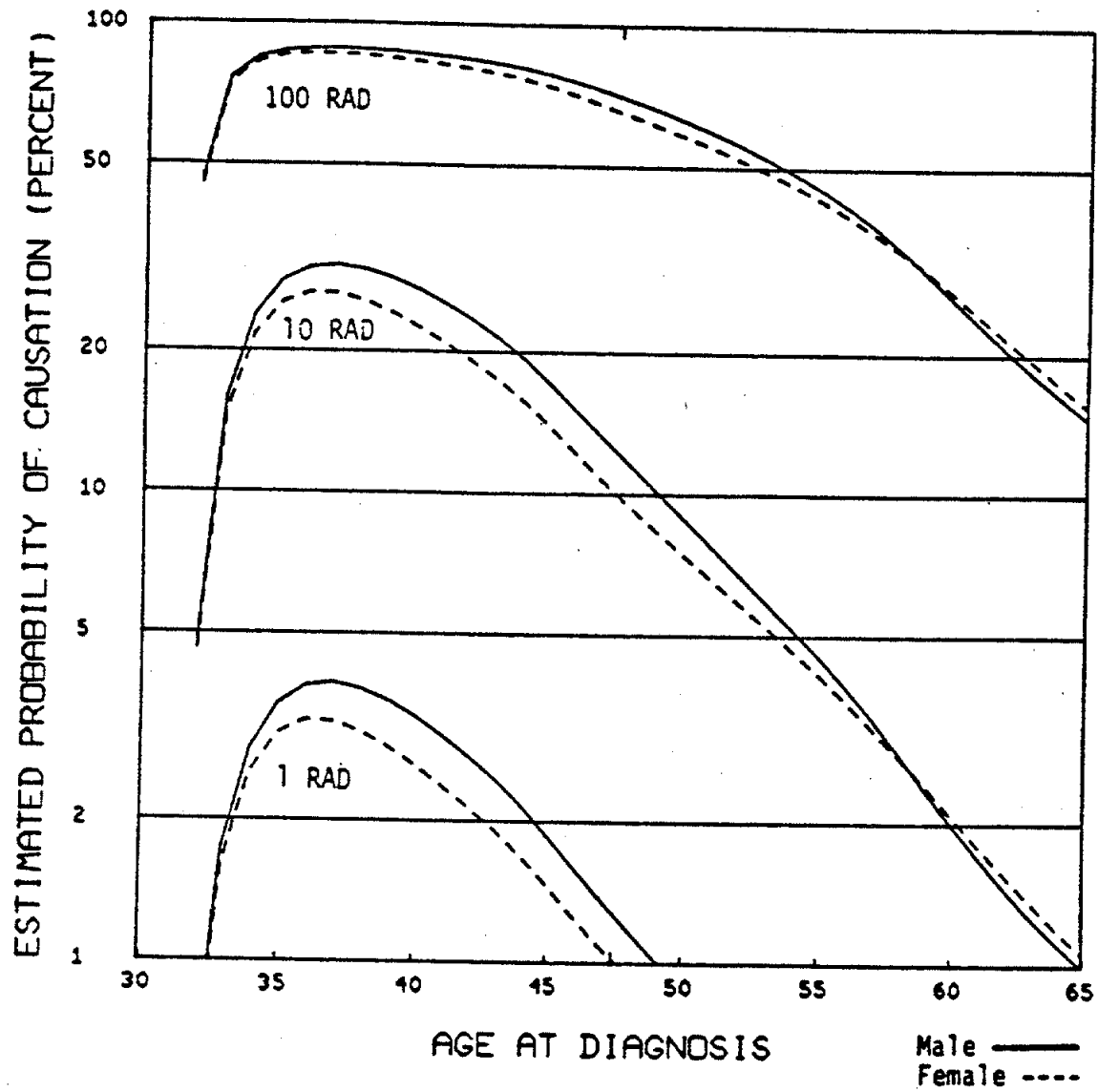
Fig X-1-C-5

LEUKEMIA: ALL TYPES EXCEPT CLL
EXPOSURE AGE 40
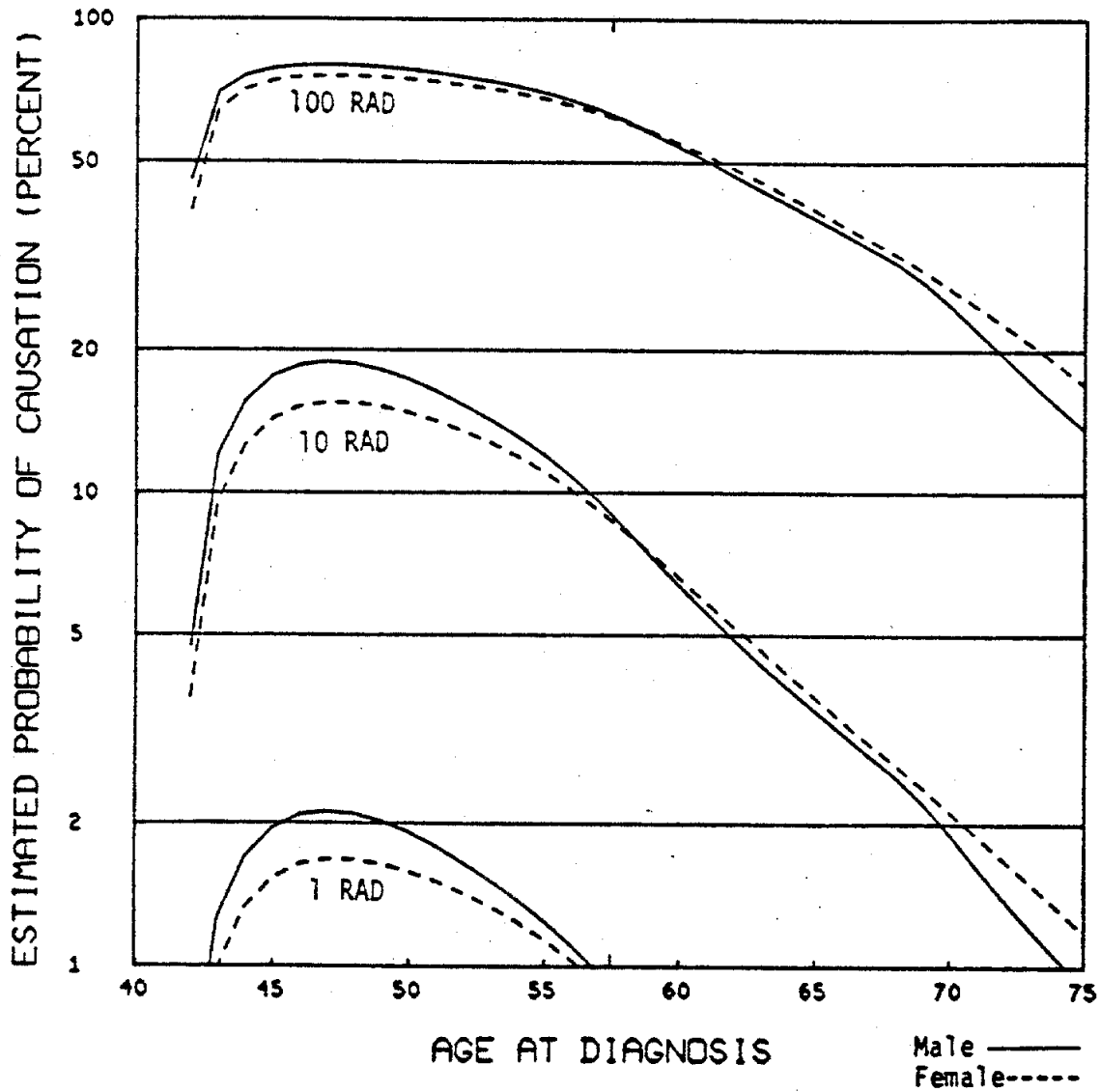
Fig X-1-C-6

LEUKEMIA: ALL TYPES EXCEPT CLL
EXPOSURE AGE 50
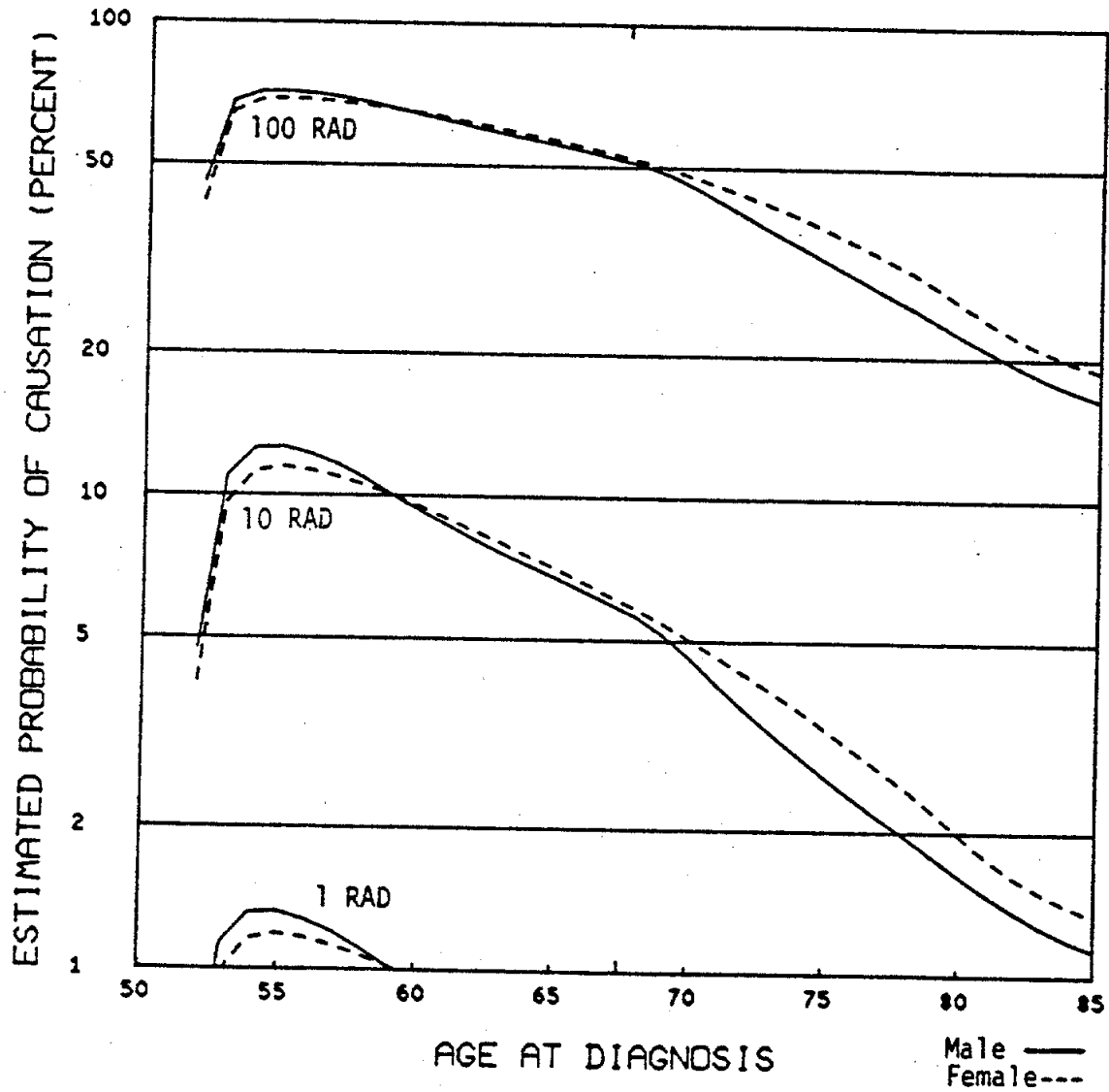
Fig X-1-C-7

LEUKEMIA: ALL TYPES EXCEPT CLL
EXPOSURE AGE 60

Fig X-1-C-8

LEUKEMIA: ALL TYPES EXCEPT CLL
EXPOSURE AGE 70
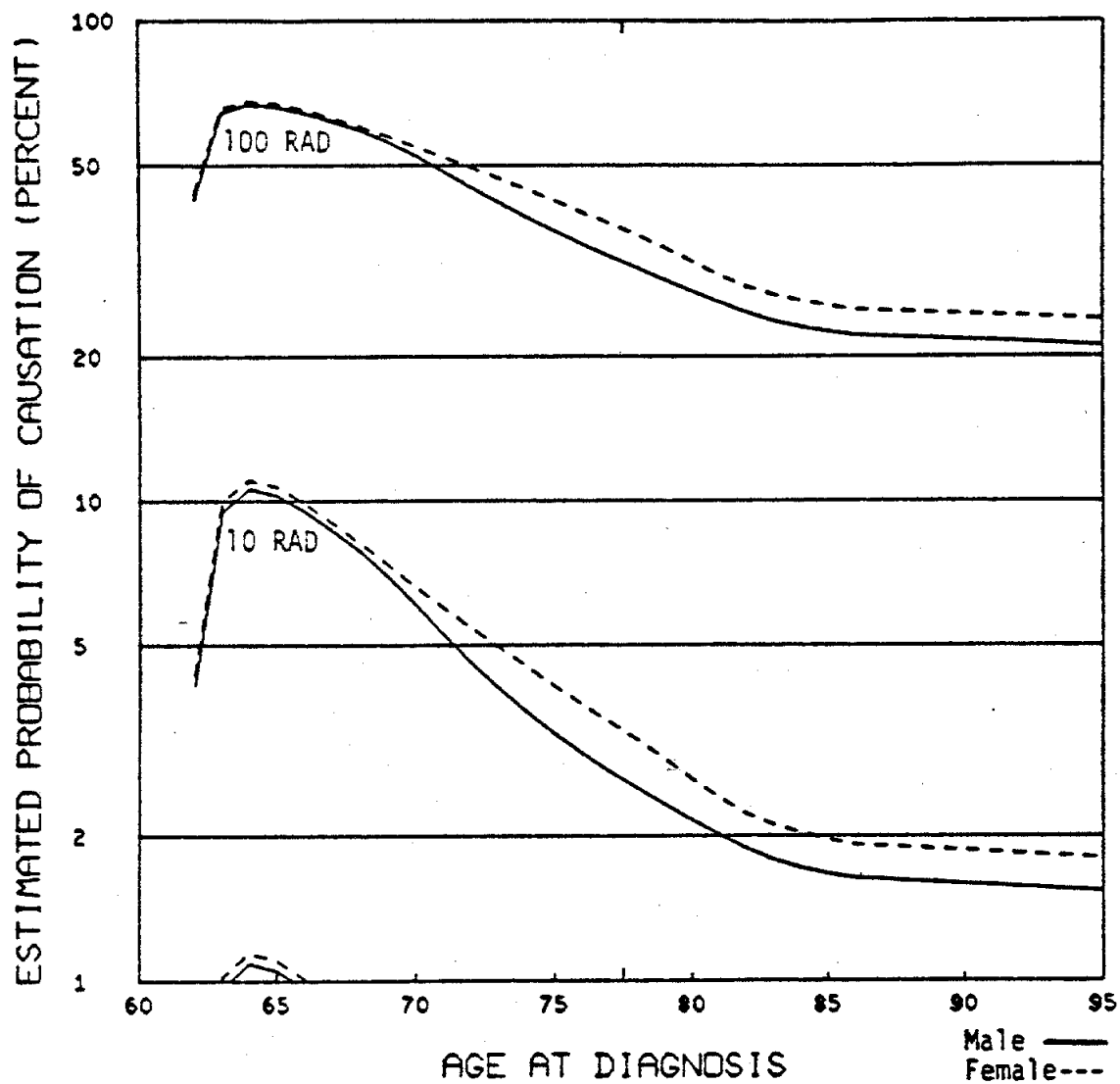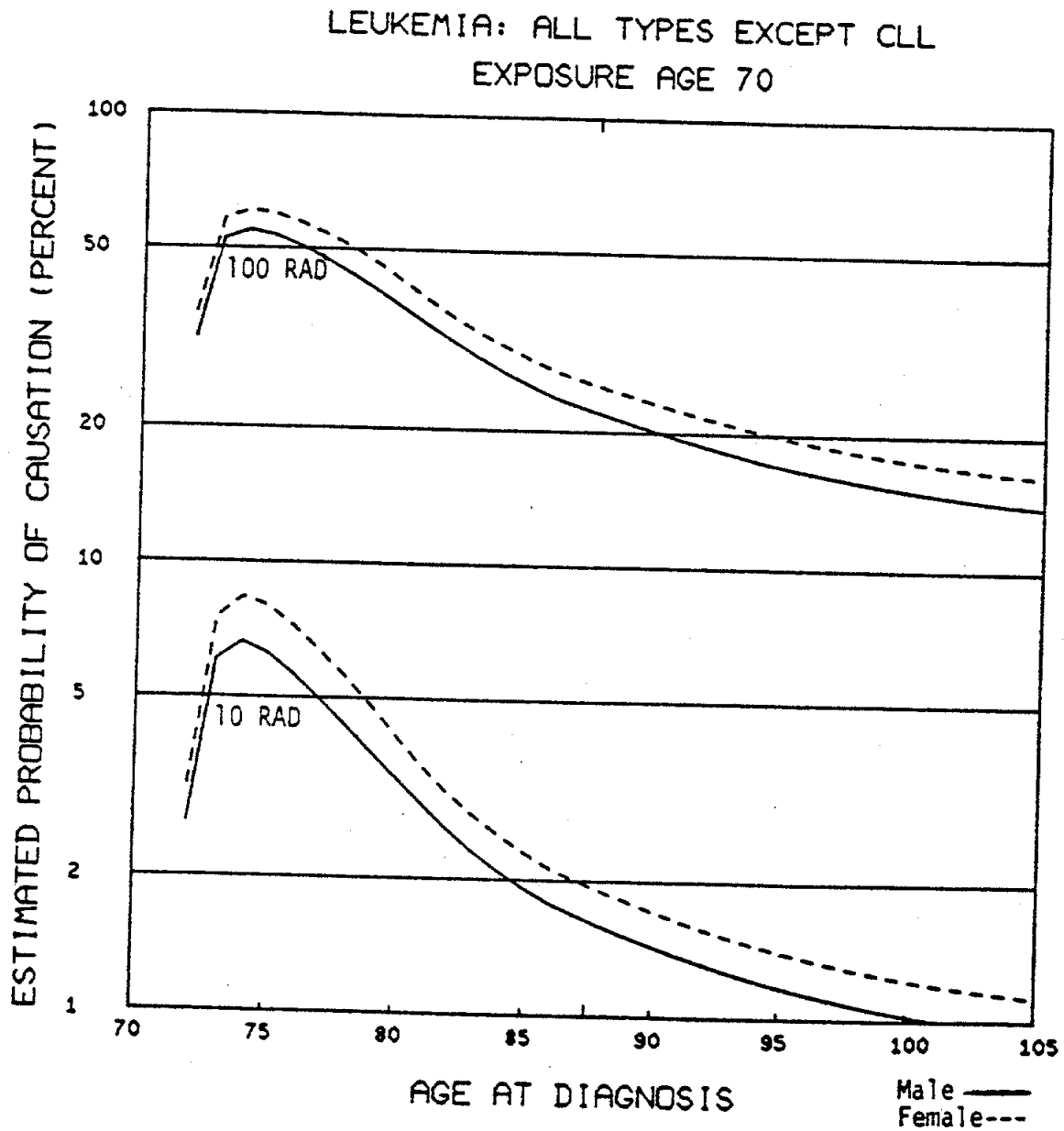
Table X-1-A. Chronic Granulocytic Leukemia:
   Temporal Distribution T(Y) by Year Y
   After Exposure

Y	T(Y)	Y	T(Y)
0	0	25	.0128
1	0	26	.0121
2	.0146	27	.0115
3	.0384	28	.0109
4	.0461	29	.0103
5	.0472	30	.00982
6	.0456	31	.00934
7	.0431	32	.00889
8	.0402	33	.00847
9	.0374	34	.00808
10	.0347	35	.00771
11	.0322	36	.00736
12	.0298	37	.00704
13	.0277	38	.00673
14	.0258	39	.00644
15	.0240	40	.00617
16	.0224	41	.00592
17	.0209	42	.00568
18	.0196	43	.00545
19	.0184	44	.00523
20	.0172	45	.00503
21	.0162	46	.00483
22	.0152	47	.00465
23	.0144	48	.00447
24	.0136	49	.00431

Table X-1-B. Chronic Granulocytic Leukemia: Risk
    Coefficient $E(A_1,S)$ by Exposure Age A_1 and Sex S

A_1	Sex		A_1	Sex	
	Male	Female		Male	Female
0	2.78	1.77	38	1.15	.742
1	2.63	1.67	39	1.17	.754
2	2.47	1.57	40	1.19	.767
3	2.31	1.47	41	1.21	.781
4	2.15	1.37	42	1.23	.795
5	1.99	1.27	43	1.25	.811
6	1.84	1.17	44	1.27	.827
7	1.69	1.08	45	1.30	.844
8	1.55	.992	46	1.32	.861
9	1.43	.911	47	1.35	.879
10	1.31	.838	48	1.38	.897
11	1.21	.775	49	1.41	.915
12	1.13	.723	50	1.43	.934
13	1.07	.684	51	1.46	.953
14	1.03	.659	52	1.49	.972
15	1.01	.647	53	1.52	.991
16	1.00	.638	54	1.55	1.01
17	.990	.631	55	1.58	1.03
18	.981	.626	56	1.61	1.05
19	.975	.622	57	1.64	1.07
20	.972	.619	58	1.67	1.09
21	.970	.618	59	1.70	1.11
22	.971	.619	60	1.73	1.12
23	.974	.621	61	1.76	1.14
24	.980	.625	62	1.78	1.16
25	.987	.630	63	1.81	1.17
26	.997	.636	64	1.84	1.19
27	1.01	.644	65	1.86	1.20
28	1.02	.653	66	1.89	1.22
29	1.03	.661	67	1.91	1.23
30	1.05	.669	68	1.94	1.25
31	1.06	.677	69	1.96	1.26
32	1.07	.685	70	1.98	1.27
33	1.08	.694	71	2.01	1.28
34	1.09	.702	72	2.03	1.29
35	1.11	.711	73	2.05	1.30
36	1.12	.721	74	2.07	1.31
37	1.13	.731	75	2.10	1.32

Table X-1-C. Chronic Granulocytic Leukemia: Baseline
Incidence $I(\lambda_2, S)$ by Age at Diagnosis λ_2 and Sex S

λ_2	Sex		λ_2	Sex	
	Male	Female		Male	Female
0	.100	.0500	43	1.12	1.01
1	.100	.0500	44	1.14	.969
2	.100	.0500	45	1.16	.918
3	.100	.0542	46	1.18	.885
4	.100	.0645	47	1.20	.900
5	.100	.0777	48	1.26	.983
6	.100	.0906	49	1.37	1.11
7	.100	.100	50	1.53	1.26
8	.100	.103	51	1.71	1.40
9	.100	.102	52	1.90	1.50
10	.100	.0984	53	2.10	1.57
11	.100	.0968	54	2.31	1.62
12	.100	.100	55	2.53	1.67
13	.106	.113	56	2.76	1.73
14	.123	.134	57	3.01	1.80
15	.147	.158	58	3.28	1.90
16	.174	.182	59	3.56	2.01
17	.200	.200	60	3.85	2.13
18	.229	.202	61	4.14	2.26
19	.265	.190	62	4.41	2.40
20	.307	.178	63	4.66	2.57
21	.352	.177	64	4.87	2.78
22	.400	.200	65	5.08	3.00
23	.477	.240	66	5.29	3.21
24	.592	.280	67	5.52	3.41
25	.719	.320	68	5.82	3.47
26	.831	.360	69	6.21	3.39
27	.900	.400	70	6.67	3.30
28	.910	.440	71	7.19	3.31
29	.878	.480	72	7.77	3.52
30	.832	.520	73	8.48	3.91
31	.797	.560	74	9.34	4.37
32	.800	.600	75	10.3	4.87
33	.838	.640	76	11.3	5.41
34	.884	.680	77	12.4	5.95
35	.931	.720	78	13.8	6.51
36	.972	.760	79	15.7	7.10
37	1.00	.800	80	17.4	7.68
38	1.02	.840	81	18.6	8.25
39	1.04	.880	82	19.0	8.78
40	1.06	.920	83	19.0	9.28
41	1.08	.960	84	19.0	9.74
42	1.10	1.00	85	19.0	10.1

Table X-1-D. Acute Leukemia: Temporal Distribution T(A₁,Y) by Year Y After Exposure at Age A₁

$T(A_1,Y)$ by Year Y After Exposure at Age A_1

Y	0	1	2	3	4	5	6	7	8
0	0	0	0	0	0	0	0	0	0
1	.0229	.0219	.0208	.0198	.0187	.0176	.0165	.0155	.0144
2	.105	.102	.0988	.0956	.0922	.0888	.0853	.0817	.0780
3	.135	.133	.131	.128	.125	.122	.119	.116	.113
4	.128	.127	.125	.124	.123	.121	.119	.117	.115
5	.109	.109	.108	.108	.107	.107	.106	.105	.104
6	.0895	.0896	.0898	.0899	.0900	.0900	.0900	.0899	.0898
7	.0723	.0728	.0732	.0736	.0741	.0745	.0748	.0752	.0755
8	.0583	.0588	.0594	.0600	.0606	.0612	.0617	.0623	.0629
9	.0470	.0476	.0482	.0488	.0495	.0502	.0508	.0515	.0522
10	.0380	.0386	.0392	.0399	.0405	.0412	.0419	.0426	.0434
11	.0309	.0315	.0321	.0327	.0333	.0340	.0347	.0354	.0361
12	.0253	.0258	.0263	.0269	.0275	.0281	.0288	.0295	.0302
13	.0208	.0213	.0217	.0223	.0228	.0234	.0240	.0246	.0253
14	.0172	.0176	.0181	.0185	.0190	.0195	.0201	.0207	.0213
15	.0143	.0147	.0151	.0155	.0159	.0164	.0169	.0175	.0180
16	.0120	.0123	.0126	.0130	.0134	.0138	.0143	.0148	.0153
17	.0100	.0103	.0106	.0110	.0113	.0117	.0121	.0126	.0130
18	.00848	.00873	.00901	.00931	.00963	.00997	.0103	.0107	.0112
19	.00719	.00741	.00766	.00792	.00821	.00852	.00885	.00920	.00958
20	.00612	.00632	.00654	.00677	.00703	.00730	.00760	.00792	.00826
21	.00523	.00541	.00560	.00581	.00604	.00629	.00655	.00684	.00715
22	.00449	.00465	.00482	.00501	.00521	.00543	.00567	.00593	.00620
23	.00387	.00401	.00416	.00433	.00451	.00471	.00492	.00515	.00540
24	.00334	.00347	.00361	.00376	.00392	.00409	.00429	.00449	.00472
25	.00290	.00301	.00313	.00327	.00341	.00357	.00374	.00393	.00413
26	.00252	.00262	.00273	.00285	.00298	.00312	.00328	.00345	.00363
27	.00220	.00229	.00239	.00250	.00261	.00274	.00288	.00303	.00320
28	.00193	.00201	.00210	.00219	.00230	.00241	.00254	.00267	.00282
29	.00169	.00176	.00184	.00193	.00202	.00213	.00224	.00236	.00250
30	.00149	.00155	.00162	.00170	.00179	.00188	.00198	.00209	.00222
31	.00131	.00137	.00144	.00151	.00158	.00167	.00176	.00186	.00197
32	.00116	.00121	.00127	.00133	.00140	.00148	.00156	.00166	.00176
33	.00103	.00108	.00113	.00119	.00125	.00132	.00139	.00148	.00157
34	.000916	.000958	.00100	.00106	.00111	.00118	.00124	.00132	.00140
35	.000815	.000853	.000896	.000943	.000994	.00105	.00111	.00118	.00126
36	.000727	.000762	.000800	.000843	.000890	.000941	.000998	.00106	.00113
37	.000650	.000682	.000716	.000755	.000798	.000845	.000896	.000954	.00102
38	.000582	.000611	.000642	.000678	.000716	.000759	.000806	.000859	.000916
39	.000522	.000548	.000577	.000609	.000644	.000684	.000727	.000774	.000827
40	.000470	.000493	.000519	.000549	.000581	.000617	.000656	.000700	.000748
41	.000423	.000444	.000468	.000495	.000524	.000557	.000593	.000633	.000677
42	.000381	.000401	.000423	.000447	.000474	.000504	.000537	.000574	.000614
43	.000344	.000362	.000382	.000405	.000429	.000457	.000487	.000521	.000558
44	.000312	.000328	.000346	.000367	.000389	.000414	.000442	.000473	.000508
45	.000282	.000297	.000314	.000333	.000353	.000377	.000402	.000431	.000462
46	.000256	.000270	.000285	.000302	.000321	.000343	.000366	.000392	.000422
47	.000233	.000245	.000259	.000275	.000293	.000312	.000334	.000358	.000385
48	.000212	.000223	.000236	.000251	.000267	.000285	.000305	.000327	.000352

- 158 -

Table X-1-D (Continued). Acute Leukemia: Temporal Distribution $f(A_i,Y)$ by Year Y After Exposure at Age A_i

A_i

Y	9	10	11	12	13	14	15	16	17
0-1	0	0	0	0	0	0	0	0	0
	0	0	0	0	0	0	0	0	0
2	.0134	.0124	.0114	.0105	.00955	.00868	.00786	.00708	.00634
3	.0743	.0706	.0669	.0631	.0594	.0557	.0520	.0484	.0449
4	.109	.104	.102	.0983	.0944	.0904	.0863	.0822	.0780
5	.113	.111	.108	.106	.103	.100	.0970	.0938	.0905
6	.103	.102	.101	.0995	.0979	.0962	.0943	.0923	.0901
7	.0895	.0892	.0888	.0882	.0876	.0868	.0859	.0849	.0837
8	.0758	.0760	.0761	.0762	.0761	.0760	.0758	.0755	.0750
9	.0634	.0640	.0644	.0649	.0652	.0655	.0658	.0659	.0660
10	.0529	.0536	.0543	.0549	.0555	.0561	.0566	.0571	.0575
11	.0441	.0449	.0457	.0464	.0472	.0479	.0486	.0492	.0498
12	.0369	.0377	.0385	.0392	.0400	.0408	.0416	.0424	.0431
13	.0309	.0317	.0325	.0332	.0341	.0349	.0357	.0365	.0373
14	.0260	.0267	.0275	.0282	.0290	.0298	.0306	.0315	.0323
15	.0220	.0226	.0233	.0241	.0248	.0256	.0264	.0272	.0280
16	.0186	.0192	.0199	.0206	.0213	.0220	.0228	.0235	.0243
17	.0158	.0164	.0170	.0176	.0183	.0190	.0197	.0204	.0212
18	.0135	.0141	.0146	.0152	.0158	.0164	.0171	.0178	.0185
19	.0116	.0121	.0126	.0131	.0137	.0143	.0149	.0155	.0162
20	.00999	.0104	.0109	.0114	.0119	.0124	.0130	.0136	.0142
21	.00863	.00902	.00943	.00987	.0103	.0108	.0114	.0119	.0125
22	.00748	.00783	.00820	.00661	.00903	.00949	.00996	.0105	.0110
23	.00650	.00682	.00716	.00752	.00791	.00833	.00877	.00923	.00973
24	.00567	.00596	.00627	.00660	.00695	.00733	.00773	.00816	.00862
25	.00496	.00522	.00550	.00580	.00612	.00647	.00684	.00723	.00765
26	.00435	.00459	.00484	.00511	.00541	.00572	.00606	.00642	.00681
27	.00383	.00404	.00427	.00452	.00479	.00508	.00539	.00572	.00607
28	.00337	.00357	.00378	.00400	.00425	.00451	.00480	.00510	.00543
29	.00298	.00316	.00335	.00356	.00378	.00402	.00428	.00456	.00486
30	.00264	.00280	.00298	.00316	.00337	.00359	.00383	.00408	.00436
31	.00235	.00249	.00265	.00282	.00301	.00321	.00343	.00367	.00392
32	.00209	.00222	.00237	.00252	.00269	.00288	.00308	.00330	.00353
33	.00187	.00199	.00212	.00226	.00241	.00258	.00277	.00297	.00319
34	.00167	.00178	.00190	.00203	.00217	.00232	.00249	.00268	.00288
35	.00149	.00159	.00170	.00182	.00195	.00210	.00225	.00242	.00261
36	.00134	.00143	.00153	.00164	.00176	.00189	.00204	.00219	.00236
37	.00121	.00129	.00138	.00148	.00159	.00171	.00184	.00199	.00214
38	.00109	.00116	.00125	.00134	.00144	.00155	.00167	.00180	.00195
39	.000980	.00105	.00113	.00121	.00130	.00141	.00152	.00164	.00178
40	.000885	.000949	.00102	.00110	.00118	.00128	.00138	.00149	.00162
41	.000801	.000860	.000925	.000996	.00107(?)	.00116	.00126	.00136	.00148
42	.000726	.000780	.000840	.000906	.000978	.00106	.00115	.00124	.00135
43	.000659	.000709	.000764	.000825	.000892	.000966	.00105	.00114	.00124
44	.000599	.000645	.000696	.000752	.000814	.000882	.000958	.00104	.00113
45	.000546	.000588	.000634	.000686	.000744	.000807	.000877	.000955	.00104
46	.000497	.000536	.000579	.000627	.000680	.000739	.000804	.000876	.000956
47	.000454	.000490	.000530	.000574	.000623	.000678	.000738	.000805	.000880
48	.000415	.000448	.000485	.000526	.000571	.000622	.000678	.000741	.000810
49	.000380	.000410	.000444	.000482	.000525	.000572	.000624	.000682	.000746

Table X-1-D (Continued). Acute Leukemia: Temporal Distribution $T(A_i,Y)$ by Year Y After Exposure at Age A_i

Y	A_i 18	19	20	21	22	23	24	25	26
1	0	0	0	0	0	0	0	0	0
2	.00566	.00502	.00443	.00389	.00340	.00295	.00255	.00219	.00187
3	.0415	.0382	.0350	.0319	.0290	.0262	.0236	.0211	.0188
4	.0738	.0696	.0654	.0612	.0571	.0531	.0491	.0452	.0414
5	.0878	.0835	.0799	.0761	.0723	.0685	.0646	.0607	.0568
6	.0878	.0853	.0827	.0799	.0770	.0739	.0708	.0675	.0642
7	.0823	.0808	.0792	.0774	.0754	.0732	.0710	.0685	.0660
8	.0744	.0737	.0728	.0718	.0706	.0693	.0678	.0662	.0643
9	.0660	.0658	.0655	.0651	.0646	.0639	.0630	.0620	.0609
10	.0578	.0581	.0582	.0582	.0581	.0579	.0576	.0571	.0565
11	.0504	.0509	.0513	.0517	.0519	.0521	.0521	.0520	.0518
12	.0438	.0445	.0451	.0456	.0461	.0465	.0468	.0470	.0471
13	.0381	.0388	.0396	.0402	.0409	.0414	.0419	.0424	.0427
14	.0331	.0339	.0347	.0354	.0362	.0369	.0375	.0380	.0385
15	.0288	.0296	.0304	.0312	.0320	.0328	.0335	.0341	.0347
16	.0251	.0259	.0267	.0275	.0283	.0291	.0299	.0306	.0313
17	.0219	.0227	.0235	.0243	.0251	.0259	.0267	.0275	.0282
18	.0192	.0200	.0207	.0215	.0223	.0231	.0239	.0246	.0254
19	.0169	.0176	.0183	.0191	.0198	.0206	.0214	.0221	.0229
20	.0148	.0155	.0162	.0169	.0176	.0184	.0191	.0199	.0207
21	.0131	.0137	.0144	.0150	.0157	.0165	.0172	.0178	.0187
22	.0116	.0122	.0128	.0134	.0141	.0147	.0154	.0162	.0169
23	.0102	.0108	.0114	.0120	.0126	.0132	.0139	.0146	.0153
24	.00910	.00961	.0101	.0107	.0113	.0119	.0125	.0132	.0139
25	.00810	.00857	.00907	.00959	.0101	.0107	.0113	.0119	.0126
26	.00722	.00766	.00812	.00861	.00912	.00967	.0102	.0108	.0114
27	.00645	.00686	.00729	.00774	.00822	.00873	.00926	.00982	.0104
28	.00578	.00615	.00655	.00698	.00743	.00790	.00840	.00893	.00948
29	.00518	.00553	.00590	.00630	.00672	.00716	.00763	.00813	.00865
30	.00466	.00498	.00532	.00569	.00608	.00650	.00694	.00741	.00790
31	.00420	.00449	.00481	.00515	.00552	.00591	.00632	.00676	.00723
32	.00379	.00406	.00436	.00467	.00501	.00538	.00577	.00618	.00662
33	.00342	.00367	.00395	.00424	.00456	.00490	.00527	.00566	.00607
34	.00310	.00333	.00359	.00386	.00416	.00448	.00482	.00518	.00557
35	.00281	.00302	.00326	.00352	.00379	.00409	.00441	.00476	.00512
36	.00255	.00275	.00297	.00321	.00347	.00374	.00404	.00437	.00471
37	.00232	.00250	.00271	.00293	.00317	.00343	.00371	.00402	.00434
38	.00211	.00228	.00247	.00268	.00290	.00315	.00341	.00370	.00400
39	.00192	.00209	.00226	.00245	.00266	.00289	.00314	.00341	.00370
40	.00176	.00191	.00207	.00225	.00245	.00266	.00289	.00314	.00342
41	.00161	.00175	.00190	.00207	.00226	.00245	.00267	.00290	.00316
42	.00147	.00160	.00174	.00190	.00207	.00226	.00246	.00268	.00293
43	.00135	.00147	.00160	.00175	.00191	.00208	.00227	.00248	.00271
44	.00124	.00135	.00147	.00161	.00176	.00192	.00210	.00230	.00252
45	.00114	.00124	.00136	.00148	.00162	.00178	.00195	.00213	.00234
46	.00104	.00114	.00125	.00137	.00150	.00165	.00181	.00198	.00217
47	.000962	.00105	.00115	.00127	.00139	.00152	.00167	.00184	.00202
48	.000887	.000972	.00107	.00117	.00129	.00141	.00155	.00171	.00188
49	.000818	.000898	.000986	.00108	.00119	.00131	.00144	.00159	.00175

Table X-1-D (Continued). Acute Leukemia: Temporal Distribution $T(A_i,Y)$ by Year Y After Exposure at Age A_i

A_i

Y	27	28	29	30	31	32	33	34	35
0	0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0	0
2	.00158	.00133	.00111	.000925	.000763	.000625	.000508	.000409	.000327
3	.0167	.0147	.0128	.0112	.00968	.00833	.00711	.00604	.00509
4	.0378	.0343	.0310	.0279	.0249	.0222	.0196	.0172	.0150
5	.0529	.0491	.0454	.0417	.0381	.0347	.0314	.0282	.0253
6	.0608	.0573	.0538	.0503	.0468	.0433	.0399	.0366	.0334
7	.0632	.0604	.0575	.0545	.0514	.0483	.0452	.0420	.0389
8	.0624	.0602	.0580	.0556	.0531	.0504	.0477	.0450	.0421
9	.0595	.0580	.0564	.0546	.0526	.0506	.0483	.0460	.0436
10	.0557	.0547	.0536	.0524	.0509	.0494	.0476	.0458	.0438
11	.0514	.0509	.0503	.0495	.0485	.0474	.0461	.0447	.0431
12	.0471	.0469	.0467	.0462	.0456	.0449	.0440	.0430	.0418
13	.0429	.0430	.0430	.0429	.0426	.0422	.0416	.0409	.0400
14	.0390	.0393	.0395	.0396	.0396	.0394	.0391	.0387	.0381
15	.0353	.0358	.0361	.0364	.0366	.0367	.0366	.0364	.0361
16	.0319	.0325	.0330	.0334	.0338	.0340	.0341	.0341	.0340
17	.0289	.0295	.0301	.0307	.0311	.0315	.0317	.0319	.0319
18	.0261	.0268	.0275	.0281	.0286	.0291	.0295	.0297	.0299
19	.0236	.0244	.0251	.0257	.0263	.0268	.0273	.0277	.0280
20	.0214	.0221	.0229	.0235	.0242	.0248	.0253	.0258	.0262
21	.0194	.0201	.0209	.0216	.0222	.0229	.0234	.0240	.0244
22	.0176	.0183	.0191	.0198	.0204	.0211	.0217	.0223	.0228
23	.0160	.0167	.0174	.0181	.0188	.0195	.0201	.0207	.0213
24	.0145	.0152	.0159	.0166	.0173	.0180	.0186	.0193	.0198
25	.0132	.0139	.0146	.0153	.0159	.0166	.0173	.0179	.0185
26	.0120	.0127	.0134	.0140	.0147	.0154	.0160	.0167	.0173
27	.0110	.0116	.0123	.0129	.0136	.0142	.0149	.0155	.0161
28	.0101	.0106	.0113	.0119	.0125	.0132	.0138	.0144	.0151
29	.00919	.00976	.0103	.0109	.0116	.0122	.0128	.0134	.0141
30	.00842	.00896	.00952	.0101	.0107	.0113	.0119	.0125	.0131
31	.00772	.00823	.00876	.00932	.00989	.0105	.0111	.0117	.0123
32	.00708	.00757	.00808	.00861	.00916	.00973	.0103	.0109	.0115
33	.00651	.00697	.00746	.00796	.00849	.00904	.00960	.0102	.0107
34	.00599	.00643	.00689	.00737	.00788	.00840	.00894	.00950	.0101
35	.00551	.00593	.00637	.00683	.00731	.00782	.00834	.00888	.00943
36	.00508	.00548	.00589	.00633	.00680	.00728	.00778	.00831	.00884
37	.00469	.00506	.00546	.00588	.00632	.00679	.00727	.00777	.00829
38	.00433	.00469	.00506	.00546	.00588	.00633	.00679	.00728	.00778
39	.00401	.00434	.00470	.00508	.00548	.00591	.00635	.00682	.00731
40	.00371	.00403	.00436	.00473	.00511	.00552	.00595	.00640	.00686
41	.00344	.00374	.00406	.00440	.00477	.00516	.00557	.00600	.00645
42	.00319	.00347	.00377	.00410	.00445	.00482	.00522	.00563	.00607
43	.00296	.00323	.00352	.00383	.00416	.00452	.00489	.00529	.00571
44	.00275	.00300	.00328	.00357	.00389	.00423	.00459	.00497	.00538
45	.00256	.00280	.00306	.00334	.00364	.00396	.00431	.00468	.00507
46	.00238	.00261	.00285	.00312	.00341	.00372	.00405	.00440	.00478
47	.00222	.00243	.00266	.00292	.00319	.00349	.00381	.00415	.00451
48	.00207	.00227	.00249	.00273	.00299	.00328	.00358	.00391	.00425
49	.00193	.00212	.00233	.00256	.00281	.00308	.00337	.00368	.00402

Table X-1-D (Continued). Acute Leukemia: Temporal Distribution $T(A_1,Y)$ by Year Y After Exposure at Age A_1

A_1

Y	36	37	38	39	40	41	42	43	44
0	0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0	0
2	.000260	.000204	.000159	.000123	.0000944	.0000717	.0000539	.0000401	.0000296
3	.00426	.00354	.00291	.00238	.00193	.00156	.00124	.000981	.000769
4	.0130	.0112	.00957	.00813	.00685	.00572	.00475	.00390	.00318
5	.0224	.0198	.0174	.0152	.0131	.0113	.00962	.00814	.00683
6	.0302	.0272	.0244	.0217	.0192	.0168	.0147	.0127	.0109
7	.0358	.0328	.0298	.0269	.0242	.0216	.0192	.0169	.0147
8	.0393	.0364	.0336	.0308	.0281	.0254	.0228	.0204	.0181
9	.0411	.0386	.0360	.0334	.0308	.0282	.0257	.0232	.0208
10	.0417	.0395	.0372	.0349	.0325	.0301	.0277	.0253	.0230
11	.0414	.0395	.0376	.0355	.0334	.0313	.0290	.0268	.0246
12	.0404	.0389	.0373	.0356	.0337	.0318	.0298	.0278	.0257
13	.0390	.0379	.0366	.0351	.0336	.0319	.0301	.0283	.0264
14	.0374	.0365	.0355	.0343	.0330	.0316	.0301	.0285	.0268
15	.0356	.0350	.0342	.0333	.0323	.0311	.0298	.0284	.0269
16	.0337	.0333	.0328	.0321	.0313	.0303	.0292	.0280	.0267
17	.0318	.0316	.0313	.0308	.0302	.0294	.0285	.0275	.0264
18	.0300	.0299	.0298	.0295	.0290	.0284	.0277	.0268	.0259
19	.0282	.0283	.0282	.0281	.0278	.0274	.0268	.0262	.0254
20	.0265	.0267	.0267	.0267	.0266	.0263	.0259	.0254	.0247
21	.0248	.0251	.0253	.0254	.0253	.0252	.0249	.0245	.0240
22	.0232	.0236	.0239	.0241	.0241	.0241	.0239	.0237	.0233
23	.0218	.0222	.0225	.0228	.0230	.0230	.0230	.0228	.0225
24	.0204	.0208	.0213	.0216	.0218	.0220	.0220	.0219	.0217
25	.0191	.0196	.0200	.0204	.0207	.0209	.0210	.0210	.0210
26	.0179	.0184	.0189	.0193	.0197	.0199	.0201	.0202	.0202
27	.0167	.0173	.0178	.0182	.0186	.0190	.0192	.0194	.0194
28	.0157	.0162	.0168	.0172	.0177	.0180	.0183	.0185	.0187
29	.0147	.0152	.0158	.0163	.0168	.0172	.0175	.0177	.0179
30	.0137	.0143	.0149	.0154	.0159	.0163	.0167	.0170	.0172
31	.0129	.0135	.0140	.0146	.0151	.0155	.0159	.0162	.0165
32	.0121	.0127	.0132	.0138	.0143	.0147	.0152	.0155	.0158
33	.0113	.0119	.0125	.0130	.0135	.0140	.0145	.0149	.0152
34	.0106	.0112	.0118	.0123	.0128	.0133	.0138	.0142	.0145
35	.00999	.0105	.0111	.0116	.0122	.0127	.0131	.0136	.0139
36	.00938	.00993	.0105	.0110	.0115	.0121	.0125	.0130	.0134
37	.00882	.00936	.00990	.0104	.0110	.0115	.0119	.0124	.0128
38	.00829	.00882	.00935	.00988	.0104	.0109	.0114	.0119	.0123
39	.00781	.00832	.00883	.00935	.00987	.0104	.0109	.0113	.0118
40	.00735	.00785	.00835	.00886	.00937	.00988	.0104	.0108	.0113
41	.00692	.00741	.00790	.00840	.00890	.00940	.00989	.0104	.0108
42	.00652	.00699	.00748	.00797	.00846	.00895	.00944	.00991	.0104
43	.00615	.00661	.00708	.00756	.00804	.00853	.00901	.00948	.00993
44	.00580	.00624	.00670	.00717	.00765	.00812	.00860	.00907	.00952
45	.00548	.00591	.00635	.00681	.00727	.00774	.00821	.00868	.00913
46	.00517	.00559	.00602	.00646	.00692	.00738	.00785	.00831	.00876
47	.00489	.00529	.00571	.00614	.00658	.00704	.00750	.00795	.00840
48	.00462	.00501	.00541	.00583	.00627	.00671	.00716	.00761	.00806
49	.00437	.00474	.00514	.00555	.00597	.00641	.00685	.00729	.00771

Table X-1-D (Continued). Acute Leukemia: Temporal Distribution $T(A_1,Y)$ by Year Y After Exposure at Age A_1

A_1

Y	45	46	47	48	49	50	51	52	53
0-1	0	0	0	0	0	0	0	0	0
2	.0000216	.0000156	.0000111	.0000078	.0000054	.0000037	.0000025	.0000017	.0000011
3	.000597	.000459	.000349	.000263	.000196	.000145	.000106	.0000762	.0000543
4	.00257	.00206	.00164	.00129	.00100	.000771	.000588	.000443	.000331
5	.00569	.00469	.00384	.00311	.00250	.00199	.00156	.00122	.000939
6	.00926	.00782	.00654	.00543	.00447	.00364	.00293	.00234	.00185
7	.0128	.0110	.00936	.00792	.00664	.00552	.00454	.00370	.00298
8	.0159	.0139	.0120	.0104	.00882	.00745	.00623	.00665	.00424
9	.0186	.0165	.0145	.0126	.0109	.00931	.00791	.00942	.00554
10	.0208	.0186	.0165	.0146	.0127	.0110	.00949	.0106	.00682
11	.0224	.0203	.0182	.0162	.0144	.0126	.0109	.0117	.00804
12	.0237	.0216	.0196	.0176	.0157	.0139	.0122	.0127	.00918
13	.0245	.0226	.0206	.0187	.0169	.0151	.0134	.0135	.0102
14	.0250	.0232	.0214	.0196	.0178	.0160	.0143	.0148	.0111
15	.0253	.0236	.0223	.0202	.0185	.0168	.0151	.0152	.0120
16	.0253	.0238	.0224	.0206	.0190	.0174	.0158	.0156	.0127
17	.0251	.0238	.0224	.0209	.0194	.0178	.0163	.0159	.0133
18	.0248	.0237	.0224	.0210	.0196	.0182	.0167	.0160	.0138
19	.0244	.0234	.0223	.0210	.0197	.0184	.0170	.0162	.0142
20	.0239	.0230	.0220	.0209	.0197	.0185	.0172	.0162	.0145
21	.0234	.0226	.0217	.0207	.0195	.0185	.0173	.0161	.0148
22	.0228	.0221	.0214	.0205	.0193	.0184	.0172	.0160	.0151
23	.0221	.0216	.0209	.0202	.0190	.0182	.0171	.0158	.0152
24	.0214	.0210	.0205	.0198	.0187	.0180	.0170	.0156	.0152
25	.0207	.0204	.0200	.0194	.0184	.0177	.0168	.0154	.0151
26	.0200	.0198	.0195	.0190	.0180	.0175	.0165	.0152	.0150
27	.0194	.0192	.0189	.0185	.0177	.0171	.0163	.0150	.0149
28	.0187	.0186	.0184	.0181	.0173	.0168	.0160	.0147	.0148
29	.0180	.0180	.0178	.0176	.0169	.0165	.0157	.0144	.0146
30	.0173	.0174	.0173	.0171	.0164	.0161	.0154	.0142	.0144
31	.0167	.0168	.0168	.0167	.0160	.0158	.0151	.0139	.0142
32	.0160	.0162	.0162	.0162	.0156	.0154	.0148	.0136	.0140
33	.0154	.0156	.0157	.0157	.0152	.0150	.0145	.0133	.0138
34	.0148	.0150	.0152	.0152	.0148	.0147	.0141	.0131	.0136
35	.0143	.0145	.0147	.0148	.0143	.0143	.0138	.0128	.0133
36	.0137	.0140	.0142	.0143	.0139	.0139	.0134	.0125	.0131
37	.0132	.0135	.0137	.0139	.0135	.0136	.0132	.0122	.0129
38	.0127	.0130	.0132	.0134	.0131	.0132	.0128	.0119	.0126
39	.0122	.0125	.0128	.0130	.0127	.0128	.0125	.0116	.0124
40	.0117	.0120	.0123	.0126	.0124	.0125	.0122	.0114	.0121
41	.0112	.0116	.0119	.0122	.0120	.0121	.0119	.0111	.0119
42	.0108	.0112	.0115	.0118	.0116	.0118	.0116	.0108	.0116
43	.0104	.0107	.0111	.0114	.0113	.0115	.0113	.0106	.0114
44	.00995	.0103	.0107	.0110	.0109	.0111	.0110	.0103	.0111
45	.00956	.00997	.0103	.0107	.0106	.0108	.0107	.0108	.0109
46	.00919	.00960	.00997	.0103	.0103	.0105	.0104	.0106	.0106
47	.00883	.00924	.00963	.00997	.00996	.0102	.0101	.0103	.0104
48	.00849	.00890	.00929	.00965	.00965	.00993			
49	.00816	.00858	.00897	.00933					

Table X-1-D (Continued). Acute Leukemia: Temporal Distribution T(A₁,Y) by Year Y After Exposure at Age A₁

A_1

Y	54	55	56	57	58	59	60	61	62
0	.0000807	0	0	0	.0000001	0	0	0	0
1	.0000383	0	0	0	.0000083	0	0	0	0
2	.000244	.0000004	.0000003	.0000001	.0000640	.0000055	.0000035	.0000023	.0000014
3	.000716	.0000266	.0000183	.0000124	.000215	.0000444	.0000304	.0000205	.0000136
4	.00145	.000178	.000128	.0000911	.000485	.000155	.000110	.0000768	.0000530
5	.00238	.000540	.000402	.000296	.000869	.000358	.000261	.000188	.000133
6	.00345	.00112	.000858	.000649	.00135	.000656	.000489	.000360	.000262
7	.00457	.00188	.00147	.00114	.00190	.00104	.000789	.000592	.000439
8	.00570	.00277	.00220	.00174	.00251	.00149	.00115	.000877	.000661
9	.00680	.00373	.00301	.00241	.00314	.00199	.00156	.00121	.000922
10	.00784	.00472	.00386	.00313	.00378	.00252	.00200	.00157	.00121
11	.00881	.00569	.00472	.00387	.00442	.00314	.00246	.00195	.00153
12	.00969	.00664	.00554	.00461	.00505	.00363	.00294	.00236	.00187
13	.0105	.00753	.00637	.00534	.00565	.00418	.00342	.00277	.00221
14	.0112	.00836	.00714	.00603	.00622	.00471	.00389	.00318	.00257
15	.0118	.00912	.00785	.00669	.00675	.00523	.00436	.00359	.00292
16	.0123	.00980	.00850	.00731	.00725	.00572	.00480	.00399	.00327
17	.0128	.0104	.00910	.00788	.00771	.00619	.00523	.00437	.00361
18	.0132	.0110	.00964	.00840	.00813	.00663	.00564	.00474	.00395
19	.0135	.0114	.0101	.00887	.00851	.00703	.00602	.00510	.00427
20	.0137	.0118	.0105	.00930	.00886	.00741	.00638	.00544	.00458
21	.0139	.0122	.0109	.00968	.00917	.00775	.00672	.00576	.00488
22	.0140	.0125	.0112	.0100	.00944	.00807	.00703	.00606	.00516
23	.0141	.0127	.0115	.0103	.00968	.00835	.00731	.00633	.00543
24	.0142	.0129	.0117	.0106	.00989	.00860	.00757	.00659	.00568
25	.0141	.0131	.0119	.0108	.0101	.00883	.00781	.00683	.00592
26	.0141	.0132	.0120	.0110	.0102	.00903	.00802	.00705	.00614
27	.0140	.0132	.0122	.0112	.0104	.00921	.00822	.00726	.00634
28	.0138	.0132	.0122	.0113	.0105	.00937	.00839	.00744	.00653
29	.0138	.0132	.0123	.0114	.0105	.00950	.00854	.00761	.00671
30	.0136	.0131	.0123	.0114	.0106	.00961	.00868	.00776	.00687
31	.0135	.0131	.0123	.0115	.0107	.00970	.00879	.00789	.00701
32	.0133	.0130	.0123	.0115	.0107	.00977	.00889	.00801	.00714
33	.0131	.0129	.0122	.0115	.0106	.00983	.00898	.00812	.00726
34	.0130	.0128	.0121	.0114	.0105	.00990	.00904	.00821	.00737
35	.0128	.0126	.0120	.0113	.0104	.00991	.00910	.00829	.00747
36	.0126	.0125	.0119	.0113	.0103	.00991	.00914	.00835	.00755
37	.0124	.0123	.0118	.0112	.0102	.00990	.00917	.00841	.00763
38	.0121	.0122	.0117	.0111	.0101	.00988	.00919	.00845	.00769
39	.0119	.0120	.0116	.0110	.0100	.00985	.00920	.00848	.00775
40	.0117	.0118	.0115	.0109	.00993	.00981	.00917	.00851	.00779
41	.0115	.0116	.0113	.0108	.00982	.00976	.00914	.00852	.00783
42	.0113	.0115	.0112	.0107	.00971	.00971	.00911	.00853	.00786
43	.0111	.0113	.0110	.0105		.00965	.00907	.00853	.00788
44	.0110	.0111	.0109	.0104		.00958	.00903	.00851	.00789
45	.0108	.0109	.0107	.0103		.00951	.00897	.00849	.00790
46	.0106	.0107	.0105	.0101		.00943	.00892	.00846	.00790
47	.0104	.0105	.0104	.0101		.00935		.00843	.00790
48		.0105	.0102	.0100					.00789
49		.0104							

Table X-1-D (Continued). Acute Leukemia: Temporal Distribution $T(A_1,Y)$ by Year Y After Exposure at Age A_1

A_1

Y	63	64	65	66	67	68	69	70	71
1	●	●	●	●	●	●	●	●	●
2	●	●	●	●	●	●	●	●	●
3	.0000009	.0000005	.0000003	.0000002	.0000001	●	●	●	●
4	.0000085	.0000057	.0000036	.0000023	.0000014	.0000008	●	.0000003	.0000001
5	.0000361	.0000242	.0000160	.0000104	.0000064	.0000042	●	.0000016	.0000009
6	.0000934	.0000645	.0000460	.0000295	.0000195	.0000127	.0000005	.0000051	.0000031
7	.000188	.000133	.0000926	.0000637	.0000431	.0000288	.0000026	.0000122	.0000077
8	.000321	.000231	.000165	.000116	.0000800	.0000545	.0000189	.0000241	.0000157
9	.000491	.000361	.000261	.000187	.000131	.0000911	.0000366	.0000419	.0000277
10	.000696	.000518	.000381	.000276	.000198	.000139	.0000967	.0000661	.0000445
11	.000929	.000702	.000523	.000384	.000279	.000199	.000131	.0000973	.0000664
12	.00119	.000906	.000684	.000509	.000374	.000270	.000193	.000135	.0000938
13	.00146	.00113	.000861	.000648	.000481	.000352	.000254	.000181	.000127
14	.00175	.00137	.00105	.000800	.000600	.000444	.000324	.000233	.000165
15	.00205	.00161	.00125	.000963	.000729	.000545	.000401	.000291	.000208
16	.00235	.00187	.00146	.00113	.000867	.000651	.000486	.000356	.000257
17	.00265	.00212	.00168	.00131	.00101	.000768	.000576	.000424	.000310
18	.00295	.00238	.00190	.00149	.00116	.000889	.000672	.000501	.000368
19	.00325	.00264	.00212	.00168	.00131	.00101	.000773	.000580	.000429
20	.00354	.00289	.00234	.00187	.00147	.00114	.000877	.000664	.000495
21	.00382	.00314	.00256	.00206	.00163	.00128	.000985	.000750	.000563
22	.00409	.00339	.00277	.00224	.00179	.00141	.00110	.000840	.000634
23	.00435	.00363	.00299	.00243	.00195	.00154	.00121	.000931	.000708
24	.00460	.00386	.00319	.00261	.00211	.00168	.00132	.00102	.000784
25	.00484	.00408	.00339	.00279	.00226	.00182	.00144	.00112	.000861
26	.00507	.00429	.00359	.00296	.00242	.00195	.00155	.00122	.000940
27	.00528	.00449	.00378	.00314	.00257	.00208	.00166	.00131	.00102
28	.00548	.00468	.00396	.00330	.00272	.00221	.00178	.00141	.00110
29	.00567	.00487	.00413	.00346	.00287	.00234	.00189	.00151	.00118
30	.00585	.00504	.00429	.00362	.00301	.00247	.00200	.00160	.00126
31	.00601	.00520	.00445	.00377	.00315	.00259	.00211	.00170	.00135
32	.00616	.00536	.00460	.00391	.00328	.00272	.00222	.00179	.00143
33	.00630	.00550	.00474	.00405	.00341	.00283	.00233	.00189	.00151
34	.00643	.00563	.00488	.00418	.00353	.00295	.00243	.00198	.00159
35	.00655	.00576	.00501	.00430	.00365	.00306	.00253	.00207	.00167
36	.00666	.00588	.00513	.00442	.00377	.00317	.00263	.00216	.00175
37	.00676	.00598	.00524	.00453	.00388	.00327	.00273	.00225	.00182
38	.00685	.00608	.00534	.00464	.00398	.00337	.00282	.00233	.00190
39	.00693	.00617	.00544	.00474	.00408	.00347	.00291	.00242	.00198
40	.00700	.00626	.00553	.00484	.00418	.00356	.00300	.00250	.00205
41	.00706	.00633	.00562	.00492	.00427	.00365	.00309	.00258	.00212
42	.00712	.00640	.00569	.00501	.00435	.00374	.00317	.00265	.00219
43	.00716	.00644	.00577	.00509	.00444	.00382	.00325	.00273	.00226
44	.00720	.00652	.00583	.00516	.00451	.00390	.00333	.00280	.00233
45	.00724	.00657	.00589	.00523	.00459	.00397	.00340	.00287	.00240
46	.00726	.00661	.00595	.00529	.00465	.00405	.00347	.00294	.00246
47	.00728	.00664	.00600	.00535	.00472	.00411	.00354	.00301	.00252
48	.00730	.00668	.00604	.00540	.00478	.00418	.00361	.00307	.00259
49	.00731	.00670	.00608	.00545	.00484	.00424	.00367	.00314	.00265

Table X-1-D (Continued). Acute Leukemia: Temporal Distribution T(A₁,Y) by Year Y After
Exposure at Age A_1

Y	A_1			
	72	73	74	75
0	0	0	0	0
1	0	0	0	0
2	0	0	0	0
3	0	0	0	0
4	0	0	0	0
5	.0000005	.0000001	.0000001	.0000001
6	.0000019	.0000011	.0000006	.0000003
7	.0000048	.0000030	.0000018	.0000010
8	.0000100	.0000063	.0000039	.0000023
9	.0000181	.0000116	.0000073	.0000045
10	.0000295	.0000192	.0000123	.0000077
11	.0000447	.0000295	.0000192	.0000123
12	.0000639	.0000428	.0000282	.0000181
13	.0000873	.0000592	.0000395	.0000259
14	.0001115	.0000788	.0000532	.0000353
15	.000147	.000102	.0000694	.0000465
16	.000183	.000128	.0000880	.0000596
17	.000222	.000157	.000109	.0000746
18	.000266	.000189	.000133	.0000916
19	.000313	.000225	.000159	.000110
20	.000363	.000263	.000187	.000131
21	.000416	.000303	.000217	.000153
22	.000472	.000346	.000250	.000178
23	.000530	.000391	.000284	.000203
24	.000591	.000439	.000321	.000231
25	.000653	.000488	.000359	.000260
26	.000717	.000538	.000398	.000290
27	.000782	.000590	.000439	.000321
28	.000848	.000644	.000481	.000354
29	.000915	.000698	.000525	.000388
30	.000983	.000753	.000569	.000423
31	.00105	.000809	.000614	.000459
32	.00112	.000866	.000660	.000495
33	.00119	.000923	.000707	.000533
34	.00126	.000980	.000754	.000571
35	.00133	.00104	.000801	.000609
36	.00139	.00110	.000849	.000648
37	.00146	.00115	.000897	.000687
38	.00153	.00121	.000945	.000727
39	.00159	.00127	.000993	.000767
40	.00166	.00132	.00104	.000807
41	.00172	.00138	.00109	.000847
42	.00179	.00144	.00114	.000888
43	.00185	.00149	.00119	.000928
44	.00191	.00155	.00123	.000968
45	.00197	.00160	.00128	.00101
46	.00203	.00165	.00133	.00105
47	.00209	.00171	.00137	.00109
48	.00215	.00176	.00142	.00113
49	.00220	.00181	.00146	.00117

Table X-1-E. Acute Leukemia: Risk Coefficient $E(A_1, S)$
by Exposure Age A_1 and Sex S

A_1	Sex Male	Sex Female	A_1	Sex Male	Sex Female
0	4.62	2.95	38	2.24	1.43
1	4.34	2.77	39	2.38	1.52
2	4.05	2.58	40	2.53	1.61
3	3.76	2.40	41	2.71	1.72
4	3.47	2.22	42	2.92	1.85
5	3.19	2.04	43	3.17	2.00
6	2.92	1.87	44	3.45	2.17
7	2.67	1.71	45	3.79	2.37
8	2.43	1.56	46	4.18	2.60
9	2.21	1.42	47	4.65	2.88
10	2.02	1.29	48	5.21	3.20
11	1.86	1.19	49	5.87	3.58
12	1.72	1.10	50	6.68	4.04
13	1.62	1.04	51	7.65	4.59
14	1.55	.992	52	8.85	5.26
15	1.52	.969	53	10.3	6.07
16	1.49	.952	54	12.2	7.08
17	1.47	.937	55	14.5	8.33
18	1.45	.926	56	17.4	9.89
19	1.44	.918	57	21.1	11.9
20	1.43	.914	58	25.9	14.4
21	1.43	.912	59	32.3	17.7
22	1.43	.914	60	40.6	22.1
23	1.44	.919	61	51.9	27.8
24	1.45	.927	62	67.2	35.5
25	1.47	.939	63	88.3	46.1
26	1.50	.955	64	118.	60.8
27	1.53	.975	65	160.	81.5
28	1.56	.998	66	221.	111.
29	1.60	1.02	67	311.	154.
30	1.64	1.05	68	445.	218.
31	1.69	1.08	69	650.	315.
32	1.74	1.11	70	969.	464.
33	1.80	1.15	71	1470.	699.
34	1.87	1.19	72	2290.	1080.
35	1.94	1.24	73	3640.	1690.
36	2.03	1.30	74	5920.	2730.
37	2.13	1.36	75	9850.	4490.

Table X-1-F. Acute Leukemia: Baseline Incidence $I(\lambda_2, S)$ by Age at Diagnosis λ_2 and Sex S

λ_2	Male	Female	λ_2	Male	Female
0	6.90	5.70	43	3.17	2.46
1	6.90	5.70	44	3.47	2.73
2	6.90	5.70	45	3.79	3.05
3	6.55	5.43	46	4.10	3.36
4	5.72	4.76	47	4.40	3.60
5	4.69	3.94	48	4.69	3.73
6	3.76	3.18	49	4.97	3.78
7	3.20	2.70	50	5.24	3.81
8	2.94	2.45	51	5.52	3.87
9	2.73	2.22	52	5.81	4.00
10	2.56	2.02	53	6.10	4.21
11	2.45	1.84	54	6.44	4.45
12	2.40	1.70	55	6.87	4.76
13	2.41	1.57	56	7.45	5.14
14	2.45	1.43	57	8.23	5.61
15	2.50	1.32	58	9.18	6.14
16	2.52	1.23	59	10.2	6.68
17	2.50	1.20	60	11.3	7.22
18	2.38	1.22	61	12.4	7.77
19	2.19	1.27	62	13.5	8.31
20	1.99	1.33	63	14.4	8.86
21	1.84	1.38	64	15.2	9.40
22	1.80	1.40	65	16.1	9.95
23	1.84	1.40	66	17.1	10.5
24	1.88	1.40	67	18.3	11.1
25	1.92	1.40	68	20.2	11.9
26	1.96	1.40	69	22.7	12.9
27	2.00	1.40	70	25.5	14.1
28	2.04	1.40	71	28.6	15.3
29	2.08	1.40	72	31.5	16.5
30	2.12	1.41	73	34.4	17.6
31	2.16	1.44	74	37.2	18.9
32	2.20	1.50	75	40.1	20.1
33	2.24	1.58	76	42.9	21.4
34	2.28	1.66	77	45.8	22.7
35	2.32	1.74	78	48.6	24.6
36	2.36	1.82	79	51.4	26.9
37	2.40	1.90	80	54.1	29.4
38	2.44	1.98	81	56.7	31.5
39	2.49	2.06	82	59.2	32.7
40	2.56	2.14	83	61.2	33.6
41	2.70	2.22	84	62.6	34.2
42	2.90	2.30	85	63.6	34.7

Table X-1-0. Leukemia, All Types Except CLL: Temporal Distribution T(A₁,Y) by Year Y After Exposure at Age A₁

A_1

Y	0	1	2	3	4	5	6	7	8
0	.0203	.0196	.0188	.0181	.0174	.0167	.0159	.0152	.0145
1	.0835	.0815	.0794	.0773	.0750	.0727	.0703	.0678	.0653
2	.107	.105	.104	.102	.0999	.0980	.0959	.0937	.0915
3	.102	.101	.100	.0994	.0984	.0972	.0962	.0949	.0935
4	.0887	.0885	.0883	.0880	.0876	.0872	.0867	.0862	.0856
5	.0746	.0747	.0748	.0749	.0750	.0750	.0750	.0749	.0748
6	.0621	.0624	.0627	.0630	.0632	.0635	.0638	.0640	.0642
7	.0516	.0520	.0524	.0527	.0531	.0536	.0540	.0543	.0547
8	.0431	.0435	.0439	.0443	.0448	.0452	.0457	.0461	.0466
9	.0362	.0366	.0370	.0374	.0378	.0383	.0388	.0393	.0398
10	.0306	.0310	.0314	.0318	.0322	.0327	.0331	.0336	.0341
11	.0261	.0264	.0268	.0272	.0276	.0280	.0284	.0289	.0294
12	.0224	.0227	.0230	.0234	.0238	.0242	.0246	.0250	.0255
13	.0194	.0197	.0200	.0203	.0206	.0210	.0214	.0218	.0222
14	.0169	.0171	.0174	.0177	.0180	.0183	.0187	.0190	.0194
15	.0148	.0150	.0153	.0155	.0158	.0161	.0164	.0167	.0171
16	.0131	.0133	.0135	.0137	.0140	.0142	.0145	.0148	.0151
17	.0116	.0118	.0120	.0122	.0124	.0127	.0129	.0132	.0135
18	.0104	.0106	.0107	.0109	.0111	.0113	.0115	.0118	.0120
19	.00934	.00948	.00963	.00979	.00996	.0101	.0104	.0106	.0108
20	.00844	.00856	.00869	.00883	.00899	.00915	.00933	.00953	.00974
21	.00765	.00776	.00788	.00800	.00814	.00829	.00845	.00863	.00882
22	.00697	.00707	.00717	.00728	.00741	.00754	.00769	.00784	.00801
23	.00637	.00646	.00655	.00665	.00676	.00688	.00701	.00716	.00731
24	.00585	.00593	.00601	.00610	.00620	.00631	.00643	.00655	.00669
25	.00539	.00546	.00553	.00561	.00570	.00580	.00590	.00602	.00614
26	.00498	.00504	.00511	.00518	.00526	.00535	.00544	.00555	.00566
27	.00462	.00467	.00473	.00480	.00487	.00495	.00503	.00513	.00523
28	.00429	.00434	.00440	.00445	.00452	.00459	.00467	.00475	.00484
29	.00400	.00405	.00409	.00415	.00420	.00427	.00434	.00441	.00450
30	.00374	.00378	.00382	.00387	.00392	.00398	.00404	.00411	.00418
31	.00350	.00354	.00358	.00362	.00367	.00372	.00377	.00384	.00390
32	.00329	.00332	.00335	.00339	.00343	.00348	.00353	.00359	.00365
33	.00309	.00312	.00315	.00319	.00322	.00327	.00331	.00336	.00342
34	.00291	.00294	.00297	.00300	.00303	.00307	.00311	.00316	.00321
35	.00275	.00277	.00280	.00283	.00286	.00289	.00293	.00297	.00302
36	.00260	.00262	.00264	.00267	.00270	.00273	.00276	.00280	.00285
37	.00246	.00248	.00250	.00252	.00255	.00258	.00261	.00265	.00269
38	.00233	.00235	.00237	.00239	.00241	.00244	.00247	.00250	.00254
39	.00221	.00223	.00225	.00227	.00229	.00231	.00234	.00237	.00240
40	.00210	.00212	.00213	.00215	.00217	.00219	.00222	.00225	.00228
41	.00200	.00202	.00203	.00205	.00207	.00209	.00211	.00213	.00216
42	.00191	.00192	.00193	.00195	.00197	.00198	.00201	.00203	.00205
43	.00182	.00183	.00184	.00186	.00187	.00189	.00191	.00193	.00195
44	.00174	.00175	.00176	.00177	.00179	.00180	.00182	.00184	.00186
45	.00166	.00167	.00168	.00169	.00171	.00172	.00174	.00175	.00177
46	.00159	.00160	.00161	.00162	.00163	.00164	.00166	.00168	.00169
47	.00152	.00153	.00154	.00155	.00156	.00157	.00159	.00160	.00162

Table X-1-G (Continued). Leukemia, All Types Except CLL: Temporal Distribution $T(A_i,Y)$ by Year Y After Exposure at Age A_i

A_i

Y	9	10	11	12	13	14	15	16	17
1	0	0	0	0	0	0	0	0	0
2	.0138	.0131	.0124	.0118	.0112	.0106	.0100	.00948	.00898
3	.0628	.0603	.0577	.0552	.0526	.0501	.0476	.0452	.0428
4	.0891	.0867	.0842	.0816	.0789	.0762	.0734	.0706	.0678
5	.0920	.0904	.0888	.0870	.0851	.0831	.0810	.0789	.0766
6	.0849	.0841	.0832	.0822	.0812	.0800	.0787	.0773	.0759
7	.0747	.0744	.0742	.0738	.0733	.0728	.0722	.0715	.0707
8	.0644	.0645	.0646	.0647	.0646	.0646	.0644	.0642	.0639
9	.0551	.0555	.0558	.0561	.0563	.0565	.0567	.0568	.0568
10	.0471	.0476	.0480	.0484	.0489	.0492	.0496	.0499	.0502
11	.0403	.0408	.0413	.0419	.0424	.0428	.0433	.0438	.0442
12	.0346	.0352	.0357	.0362	.0368	.0373	.0378	.0384	.0389
13	.0299	.0304	.0309	.0315	.0320	.0326	.0331	.0337	.0342
14	.0259	.0264	.0269	.0275	.0280	.0285	.0291	.0296	.0302
15	.0226	.0231	.0236	.0240	.0246	.0251	.0256	.0262	.0267
16	.0198	.0202	.0207	.0212	.0216	.0221	.0226	.0232	.0237
17	.0175	.0179	.0183	.0187	.0191	.0196	.0201	.0206	.0211
18	.0155	.0158	.0162	.0166	.0170	.0174	.0179	.0184	.0188
19	.0138	.0141	.0144	.0148	.0152	.0156	.0160	.0164	.0169
20	.0123	.0126	.0129	.0132	.0136	.0140	.0143	.0147	.0152
21	.0110	.0113	.0116	.0119	.0122	.0125	.0129	.0133	.0137
22	.00996	.0102	.0105	.0107	.0110	.0113	.0117	.0120	.0124
23	.00902	.00923	.00947	.00971	.00998	.0103	.0106	.0109	.0112
24	.00819	.00839	.00860	.00883	.00907	.00932	.00960	.00989	.0102
25	.00747	.00765	.00784	.00805	.00826	.00850	.00875	.00902	.00930
26	.00684	.00700	.00717	.00736	.00756	.00777	.00800	.00825	.00851
27	.00628	.00642	.00658	.00675	.00693	.00713	.00734	.00756	.00780
28	.00578	.00591	.00605	.00621	.00637	.00655	.00675	.00695	.00718
29	.00534	.00546	.00558	.00573	.00588	.00604	.00622	.00641	.00661
30	.00494	.00505	.00517	.00529	.00543	.00558	.00574	.00592	.00611
31	.00459	.00468	.00479	.00491	.00503	.00517	.00532	.00548	.00565
32	.00427	.00436	.00445	.00456	.00468	.00480	.00494	.00509	.00525
33	.00398	.00406	.00415	.00425	.00435	.00448	.00459	.00473	.00488
34	.00372	.00379	.00387	.00396	.00406	.00417	.00428	.00441	.00454
35	.00348	.00355	.00362	.00371	.00379	.00389	.00400	.00411	.00424
36	.00327	.00333	.00340	.00347	.00355	.00364	.00374	.00385	.00396
37	.00307	.00313	.00319	.00326	.00333	.00342	.00351	.00360	.00371
38	.00289	.00294	.00300	.00306	.00313	.00321	.00329	.00338	.00348
39	.00273	.00278	.00283	.00289	.00295	.00302	.00309	.00318	.00327
40	.00258	.00262	.00267	.00272	.00278	.00284	.00291	.00299	.00308
41	.00244	.00248	.00252	.00257	.00262	.00268	.00275	.00282	.00290
42	.00231	.00235	.00239	.00243	.00248	.00254	.00260	.00266	.00274
43	.00219	.00223	.00226	.00230	.00235	.00240	.00246	.00252	.00258
44	.00208	.00211	.00215	.00219	.00223	.00227	.00233	.00238	.00245
45	.00198	.00201	.00204	.00208	.00212	.00216	.00220	.00226	.00232
46	.00188	.00191	.00194	.00197	.00201	.00205	.00209	.00214	.00220
47	.00180	.00182	.00185	.00188	.00191	.00195	.00199	.00204	.00209
48	.00171	.00174	.00176	.00179	.00182	.00185	.00189	.00194	.00198
49	.00164	.00166	.00168	.00171	.00174	.00177	.00180	.00184	.00189

Table X-1-G (Continued). Leukemia, All Types Except CLL: Temporal Distribution T(A₁,Y) by Year Y After Exposure at Age A₁

$$A_1$$

Y	18	19	20	21	22	23	24	25	26
0	0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0	0
2	.00852	.00808	.00868	.00732	.00698	.00668	.00640	.00616	.00594
3	.0405	.0382	.0361	.0340	.0320	.0301	.0283	.0266	.0251
4	.0649	.0621	.0592	.0564	.0536	.0508	.0481	.0455	.0429
5	.0743	.0719	.0694	.0669	.0643	.0617	.0590	.0564	.0537
6	.0698	.0726	.0708	.0684	.0669	.0636	.0627	.0605	.0582
7	.0635	.0688	.0676	.0664	.0650	.0600	.0620	.0604	.0586
8	.0568	.0630	.0624	.0617	.0609	.0554	.0590	.0579	.0566
9	.0504	.0567	.0565	.0562	.0559	.0505	.0548	.0541	.0533
10	.0446	.0506	.0507	.0507	.0506	.0457	.0503	.0499	.0495
11	.0393	.0449	.0452	.0454	.0456	.0412	.0457	.0457	.0455
12	.0348	.0398	.0402	.0406	.0409	.0370	.0414	.0415	.0416
13	.0308	.0353	.0358	.0362	.0367	.0333	.0374	.0377	.0379
14	.0273	.0313	.0318	.0324	.0328	.0300	.0337	.0341	.0345
15	.0242	.0278	.0284	.0289	.0294	.0270	.0304	.0309	.0313
16	.0216	.0248	.0253	.0259	.0264	.0243	.0275	.0280	.0285
17	.0193	.0222	.0227	.0232	.0238	.0220	.0249	.0254	.0259
18	.0173	.0198	.0204	.0209	.0214	.0199	.0225	.0230	.0235
19	.0156	.0178	.0183	.0188	.0194	.0180	.0204	.0209	.0214
20	.0141	.0161	.0165	.0170	.0175	.0164	.0185	.0190	.0196
21	.0127	.0145	.0150	.0154	.0159	.0149	.0169	.0174	.0179
22	.0116	.0131	.0136	.0140	.0144	.0136	.0154	.0159	.0164
23	.0105	.0119	.0123	.0127	.0132	.0124	.0141	.0145	.0150
24	.00961	.0109	.0112	.0116	.0120	.0114	.0129	.0133	.0138
25	.00879	.00993	.0103	.0106	.0110	.0105	.0118	.0122	.0127
26	.00806	.00909	.00940	.00973	.0101	.00961	.0108	.0112	.0117
27	.00741	.00834	.00863	.00894	.00927	.00886	.00997	.0104	.0107
28	.00683	.00767	.00794	.00823	.00853	.00818	.00920	.00956	.00993
29	.00631	.00707	.00732	.00759	.00787	.00756	.00850	.00883	.00919
30	.00584	.00653	.00676	.00701	.00728	.00701	.00786	.00818	.00852
31	.00542	.00604	.00626	.00649	.00674	.00650	.00729	.00759	.00790
32	.00504	.00561	.00581	.00602	.00625	.00604	.00677	.00705	.00735
33	.00469	.00521	.00540	.00560	.00581	.00563	.00629	.00656	.00684
34	.00438	.00485	.00502	.00521	.00541	.00525	.00586	.00611	.00637
35	.00409	.00452	.00468	.00486	.00505	.00490	.00547	.00570	.00595
36	.00383	.00423	.00438	.00454	.00471	.00459	.00511	.00533	.00556
37	.00359	.00396	.00409	.00424	.00441	.00430	.00478	.00498	.00520
38	.00337	.00371	.00384	.00398	.00413	.00403	.00447	.00467	.00488
39	.00317	.00348	.00360	.00373	.00387	.00378	.00420	.00438	.00458
40	.00299	.00327	.00338	.00351	.00364	.00356	.00394	.00411	.00430
41	.00282	.00308	.00318	.00330	.00342	.00335	.00371	.00387	.00404
42	.00266	.00290	.00300	.00311	.00322	.00316	.00349	.00364	.00381
43	.00251	.00274	.00283	.00293	.00304	.00298	.00329	.00343	.00359
44	.00238	.00259	.00268	.00277	.00287	.00282	.00310	.00324	.00338
45	.00226	.00245	.00253	.00262	.00271	.00267	.00293	.00306	.00320
46	.00214	.00232	.00240	.00248	.00257	.00252	.00277	.00289	.00302
47	.00203	.00220	.00227	.00235	.00243	.00239	.00263	.00274	.00286
48	.00193	.00209	.00216	.00223	.00231	.00227	.00249	.00259	.00271
49		.00199	.00205	.00212	.00219		.00236	.00246	.00257

Table X-1-0 (Continued). Leukemia, All Types Except CLL: Temporal Distribution $T(A_i, Y)$ by Year Y After Exposure at Age A_i

Y	A_i = 27	28	29	30	31	32	33	34	35
0	0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0	0
2	.00575	.00558	.00543	.00530	.00519	.00509	.00502	.00495	.00489
3	.0236	.0223	.0210	.0199	.0189	.0179	.0171	.0164	.0157
4	.0405	.0381	.0359	.0337	.0317	.0298	.0281	.0264	.0250
5	.0511	.0485	.0459	.0434	.0410	.0387	.0364	.0343	.0323
6	.0559	.0536	.0512	.0468	.0464	.0441	.0418	.0395	.0373
7	.0568	.0549	.0529	.0508	.0488	.0466	.0445	.0424	.0402
8	.0553	.0538	.0523	.0507	.0489	.0472	.0453	.0434	.0415
9	.0524	.0514	.0503	.0491	.0478	.0463	.0448	.0433	.0416
10	.0490	.0483	.0476	.0467	.0457	.0447	.0435	.0422	.0409
11	.0453	.0449	.0445	.0439	.0433	.0425	.0416	.0407	.0396
12	.0416	.0415	.0413	.0410	.0406	.0401	.0395	.0388	.0379
13	.0380	.0381	.0381	.0380	.0378	.0376	.0372	.0367	.0361
14	.0347	.0350	.0351	.0352	.0352	.0350	.0349	.0346	.0342
15	.0317	.0320	.0323	.0324	.0326	.0326	.0326	.0324	.0322
16	.0289	.0293	.0296	.0299	.0301	.0303	.0304	.0304	.0303
17	.0263	.0268	.0272	.0275	.0278	.0281	.0283	.0284	.0284
18	.0240	.0245	.0250	.0254	.0257	.0260	.0263	.0265	.0266
19	.0220	.0224	.0229	.0234	.0238	.0241	.0244	.0247	.0249
20	.0201	.0206	.0211	.0215	.0220	.0224	.0227	.0230	.0233
21	.0184	.0189	.0194	.0198	.0203	.0207	.0211	.0215	.0218
22	.0168	.0173	.0178	.0183	.0188	.0192	.0196	.0200	.0204
23	.0155	.0160	.0164	.0169	.0174	.0178	.0183	.0187	.0191
24	.0142	.0147	.0152	.0156	.0161	.0166	.0170	.0174	.0178
25	.0131	.0136	.0140	.0145	.0149	.0154	.0158	.0163	.0167
26	.0121	.0125	.0130	.0134	.0139	.0143	.0148	.0152	.0156
27	.0112	.0116	.0120	.0124	.0129	.0133	.0138	.0142	.0146
28	.0103	.0107	.0111	.0116	.0120	.0124	.0129	.0133	.0137
29	.00956	.00994	.0103	.0107	.0112	.0116	.0120	.0124	.0129
30	.00887	.00923	.00961	.0100	.0104	.0108	.0112	.0117	.0121
31	.00824	.00858	.00895	.00933	.00971	.0101	.0105	.0109	.0113
32	.00766	.00799	.00834	.00870	.00907	.00946	.00985	.0103	.0107
33	.00714	.00745	.00778	.00813	.00848	.00886	.00924	.00963	.0100
34	.00664	.00695	.00727	.00760	.00794	.00830	.00867	.00904	.00943
35	.00622	.00650	.00680	.00711	.00744	.00778	.00814	.00868	.00888
36	.00581	.00608	.00636	.00666	.00698	.00731	.00765	.00800	.00837
37	.00544	.00570	.00594	.00625	.00655	.00687	.00720	.00754	.00789
38	.00510	.00534	.00560	.00587	.00616	.00646	.00677	.00710	.00744
39	.00479	.00501	.00526	.00552	.00579	.00608	.00638	.00670	.00703
40	.00450	.00471	.00494	.00519	.00545	.00573	.00602	.00632	.00664
41	.00423	.00443	.00465	.00489	.00514	.00540	.00568	.00597	.00628
42	.00398	.00418	.00438	.00461	.00485	.00510	.00536	.00565	.00594
43	.00375	.00394	.00413	.00434	.00457	.00481	.00507	.00534	.00563
44	.00354	.00372	.00390	.00410	.00432	.00455	.00480	.00507	.00533
45	.00335	.00351	.00369	.00388	.00408	.00430	.00454	.00479	.00505
46	.00316	.00332	.00349	.00367	.00386	.00407	.00430	.00454	.00480
47	.00299	.00314	.00330	.00347	.00366	.00386	.00408	.00431	.00455
48	.00284	.00297	.00313	.00329	.00347	.00366	.00387	.00409	.00432
49	.00269	.00282	.00296	.00312	.00329	.00347	.00367	.00388	.00411

Table X-1-G (Continued). Leukemia, All Types Except CLL: Temporal Distribution T(A_1,Y) by Year Y After Exposure at Age A_1

Y	\(A_1\)								
	36	37	38	39	40	41	42	43	44
0	0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0	0
2	.00485	.00481	.00478	.00475	.00473	.00472	.00471	.00470	.00469
3	.0152	.0147	.0143	.0139	.0136	.0133	.0131	.0129	.0128
4	.0236	.0224	.0213	.0203	.0194	.0186	.0180	.0174	.0169
5	.0304	.0286	.0269	.0254	.0240	.0228	.0216	.0206	.0197
6	.0352	.0331	.0312	.0293	.0276	.0260	.0246	.0232	.0220
7	.0381	.0361	.0340	.0321	.0302	.0285	.0268	.0252	.0238
8	.0396	.0376	.0357	.0347	.0320	.0301	.0284	.0267	.0252
9	.0399	.0382	.0364	.0348	.0329	.0311	.0294	.0278	.0261
10	.0394	.0380	.0364	.0345	.0332	.0316	.0299	.0283	.0267
11	.0384	.0372	.0358	.0337	.0330	.0315	.0300	.0285	.0270
12	.0370	.0360	.0349	.0328	.0325	.0312	.0298	.0284	.0268
13	.0354	.0346	.0337	.0316	.0317	.0306	.0294	.0281	.0265
14	.0346	.0337	.0324	.0303	.0307	.0298	.0287	.0276	.0259
15	.0337	.0331	.0309	.0290	.0296	.0288	.0279	.0270	.0253
16	.0319	.0315	.0295	.0276	.0284	.0278	.0271	.0262	.0246
17	.0301	.0298	.0280	.0263	.0272	.0267	.0261	.0254	.0239
18	.0284	.0282	.0265	.0250	.0260	.0256	.0251	.0246	.0231
19	.0267	.0266	.0251	.0237	.0248	.0245	.0241	.0237	.0223
20	.0250	.0251	.0237	.0224	.0236	.0234	.0231	.0228	.0215
21	.0235	.0236	.0224	.0212	.0224	.0223	.0221	.0219	.0207
22	.0220	.0222	.0211	.0201	.0213	.0213	.0212	.0210	.0199
23	.0207	.0209	.0199	.0190	.0202	.0202	.0202	.0201	.0191
24	.0194	.0197	.0188	.0180	.0192	.0193	.0193	.0192	.0183
25	.0182	.0185	.0177	.0170	.0182	.0183	.0184	.0184	.0176
26	.0171	.0174	.0167	.0161	.0172	.0174	.0176	.0176	.0169
27	.0160	.0164	.0158	.0152	.0164	.0166	.0167	.0168	.0162
28	.0150	.0154	.0149	.0144	.0155	.0158	.0159	.0161	.0155
29	.0141	.0145	.0140	.0136	.0147	.0150	.0152	.0154	.0148
30	.0133	.0137	.0133	.0129	.0139	.0142	.0145	.0147	.0142
31	.0125	.0129	.0125	.0122	.0132	.0135	.0138	.0140	.0136
32	.0117	.0121	.0118	.0116	.0126	.0129	.0132	.0134	.0130
33	.0111	.0115	.0112	.0110	.0119	.0122	.0125	.0128	.0125
34	.0104	.0108	.0106	.0104	.0113	.0117	.0120	.0122	.0119
35	.00982	.0102	.0100	.00985	.0107	.0111	.0114	.0117	.0114
36	.00926	.00964	.00948	.00935	.0102	.0106	.0109	.0112	.0110
37	.00874	.00911	.00898	.00887	.00970	.0100	.0104	.0107	.0105
38	.00825	.00861	.00851	.00842	.00923	.00957	.00990	.0102	.0101
39	.00779	.00815	.00807	.00800	.00878	.00912	.00945	.00977	.00964
40	.00737	.00772	.00766	.00761	.00835	.00869	.00903	.00894	.00924
41	.00697	.00731	.00727	.00723	.00795	.00829	.00862	.00856	.00886
42	.00660	.00693	.00690	.00688	.00757	.00790	.00823	.00819	.00850
43	.00625	.00657	.00655	.00655	.00721	.00754	.00787	.00784	.00815
44	.00593	.00624	.00623	.00624	.00687	.00720	.00752	.00751	.00782
45	.00562	.00592	.00593	.00594	.00655	.00687	.00719	.00719	.00750
46	.00533	.00562	.00564	.00564	.00625	.00657	.00688	.00689	.00720
47	.00506	.00535	.00537	.00540	.00597	.00627	.00658	.00661	.00691
48	.00481	.00508	.00511	.00515	.00569	.00600	.00630	.00634	.00664
49	.00457	.00484	.00487		.00544	.00573	.00603		

- 173 -

Table X-1-0 (Continued). Leukemia, All Types Except CLL: Temporal Distribution T(A_i,Y) by Year Y After Exposure at Age A_i

A_i

Y	45	46	47	48	49	50	51	52	53
0	0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0	0
2	.00468	.00468	.00468	.00468	.00467	.00467	.00467	.00467	.00467
3	.0127	.0126	.0125	.0125	.0124	.0124	.0123	.0123	.0123
4	.0165	.0162	.0159	.0156	.0154	.0153	.0152	.0151	.0150
5	.0190	.0183	.0177	.0172	.0168	.0164	.0162	.0159	.0157
6	.0209	.0199	.0190	.0183	.0176	.0171	.0166	.0162	.0159
7	.0225	.0212	.0202	.0192	.0183	.0179	.0169	.0163	.0158
8	.0237	.0223	.0211	.0199	.0189	.0183	.0171	.0164	.0157
9	.0246	.0232	.0218	.0205	.0194	.0186	.0173	.0165	.0157
10	.0252	.0237	.0223	.0210	.0198	.0188	.0176	.0166	.0158
11	.0255	.0241	.0227	.0213	.0201	.0190	.0177	.0167	.0158
12	.0256	.0242	.0229	.0215	.0202	.0191	.0179	.0168	.0158
13	.0255	.0242	.0229	.0216	.0203	.0191	.0180	.0169	.0158
14	.0253	.0240	.0228	.0216	.0203	.0190	.0179	.0169	.0158
15	.0249	.0238	.0226	.0214	.0201	.0188	.0178	.0168	.0158
16	.0244	.0234	.0223	.0212	.0199	.0186	.0176	.0167	.0157
17	.0238	.0229	.0219	.0209	.0196	.0184	.0174	.0166	.0156
18	.0232	.0224	.0215	.0206	.0193	.0181	.0172	.0165	.0155
19	.0225	.0218	.0210	.0202	.0189	.0178	.0170	.0163	.0154
20	.0218	.0212	.0205	.0197	.0186	.0174	.0167	.0161	.0152
21	.0212	.0206	.0200	.0193	.0182	.0170	.0164	.0159	.0150
22	.0211	.0199	.0194	.0188	.0177	.0167	.0161	.0156	.0148
23	.0203	.0193	.0188	.0183	.0173	.0163	.0157	.0154	.0146
24	.0196	.0186	.0183	.0178	.0168	.0159	.0154	.0151	.0144
25	.0189	.0180	.0177	.0173	.0164	.0155	.0151	.0148	.0142
26	.0182	.0173	.0171	.0168	.0159	.0151	.0147	.0145	.0139
27	.0175	.0167	.0165	.0163	.0155	.0147	.0144	.0142	.0137
28	.0168	.0161	.0160	.0158	.0150	.0143	.0140	.0139	.0134
29	.0162	.0155	.0154	.0153	.0146	.0143	.0137	.0136	.0132
30	.0155	.0149	.0149	.0148	.0142	.0142	.0133	.0133	.0129
31	.0149	.0144	.0144	.0143	.0137	.0136	.0130	.0130	.0126
32	.0143	.0138	.0139	.0138	.0133	.0132	.0126	.0127	.0124
33	.0138	.0133	.0134	.0134	.0129	.0128	.0123	.0124	.0121
34	.0132	.0128	.0129	.0129	.0125	.0124	.0120	.0121	.0118
35	.0127	.0123	.0124	.0125	.0121	.0121	.0116	.0118	.0116
36	.0122	.0118	.0120	.0121	.0117	.0117	.0113	.0115	.0113
37	.0117	.0114	.0116	.0117	.0114	.0114	.0110	.0112	.0111
38	.0112	.0110	.0112	.0113	.0110	.0110	.0107	.0109	.0108
39	.0108	.0106	.0108	.0109	.0106	.0107	.0104	.0107	.0105
40	.0103	.0102	.0104	.0105	.0103	.0104	.0101	.0104	.0103
41	.00992	.00977	.00999	.0102	.00997	.0101	.00984	.0101	.0100
42	.00952	.00940	.00963	.00982	.00965	.00977	.00956	.00985	.00981
43	.00915	.00905	.00929	.00949	.00934	.00947	.00929	.00959	.00957
44	.00879	.00871	.00896	.00917	.00904	.00919	.00902	.00934	.00934
45	.00844	.00839	.00864	.00886	.00875	.00891	.00877	.00909	.00911
46	.00811	.00807	.00833	.00856	.00847	.00864	.00852	.00885	.00888
47	.00779	.00777	.00804	.00827	.00820	.00838	.00828	.00862	.00866
48	.00749	.00749	.00775	.00799	.00794	.00813		.00839	.00845
49	.00693	.00721	.00748	.00772					

- 174 -

Table X-1-G (Continued). Leukemia, All Types Except CLL; Temporal Distribution T(A₁,Y) by Year Y After Exposure at Age A₁

A_1

Y	54	55	56	57	58	59	60	61	62
0	0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0	0
2	.00467	.00467	.00467	.00467	.00467	.00467	.00467	.00467	.00467
3	.0123	.0123	.0123	.0123	.0123	.0123	.0123	.0123	.0123
4	.0149	.0149	.0148	.0148	.0148	.0148	.0148	.0148	.0148
5	.0156	.0155	.0154	.0153	.0152	.0152	.0152	.0151	.0151
6	.0156	.0154	.0152	.0150	.0149	.0148	.0141	.0147	.0147
7	.0154	.0151	.0148	.0146	.0144	.0142	.0141	.0140	.0140
8	.0152	.0148	.0144	.0141	.0138	.0136	.0134	.0133	.0132
9	.0151	.0145	.0140	.0136	.0133	.0130	.0127	.0126	.0124
10	.0150	.0143	.0137	.0132	.0128	.0125	.0122	.0119	.0117
11	.0149	.0142	.0135	.0129	.0124	.0120	.0117	.0114	.0111
12	.0149	.0141	.0133	.0127	.0121	.0116	.0112	.0109	.0106
13	.0149	.0140	.0132	.0125	.0119	.0113	.0109	.0105	.0101
14	.0148	.0139	.0131	.0124	.0117	.0111	.0106	.0101	.00975
15	.0148	.0139	.0130	.0122	.0115	.0109	.0103	.00961	.00943
16	.0147	.0138	.0130	.0121	.0114	.0107	.0101	.00941	.00915
17	.0147	.0137	.0129	.0121	.0113	.0106	.00996	.00924	.00892
18	.0146	.0136	.0128	.0120	.0112	.0105	.00982	.00910	.00872
19	.0145	.0136	.0128	.0119	.0111	.0104	.00971	.00898	.00856
20	.0143	.0135	.0127	.0118	.0110	.0103	.00952	.00888	.00842
21	.0142	.0134	.0125	.0117	.0109	.0102	.00944	.00879	.00830
22	.0140	.0132	.0124	.0116	.0108	.0101	.00938	.00872	.00820
23	.0139	.0131	.0124	.0115	.0108	.0101	.00931	.00865	.00811
24	.0137	.0130	.0125	.0114	.0107	.0100	.00925	.00858	.00803
25	.0135	.0128	.0124	.0113	.0106	.00995	.00919	.00853	.00796
26	.0133	.0126	.0121	.0112	.0105	.00989	.00913	.00847	.00790
27	.0131	.0125	.0119	.0111	.0104	.00982	.00907	.00842	.00785
28	.0129	.0123	.0118	.0110	.0103	.00975	.00901	.00837	.00780
29	.0127	.0121	.0117	.0109	.0102	.00968	.00895	.00832	.00775
30	.0124	.0119	.0115	.0108	.0102	.00960	.00889	.00826	.00770
31	.0122	.0117	.0114	.0106	.0100	.00952	.00882	.00821	.00766
32	.0120	.0115	.0112	.0105	.00994	.00944	.00876	.00816	.00761
33	.0118	.0113	.0110	.0102	.00983	.00936	.00869	.00810	.00757
34	.0115	.0111	.0109	.0101	.00972	.00927	.00862	.00805	.00752
35	.0113	.0109	.0107	.00995	.00961	.00918	.00854	.00799	.00748
36	.0111	.0107	.0105	.00966	.00949	.00909	.00847	.00793	.00743
37	.0108	.0105	.0102	.00951	.00937	.00899	.00839	.00787	.00739
38	.0106	.0103	.0100	.00936	.00925	.00889	.00831	.00781	.00734
39	.0104	.0101	.00981	.00921	.00912	.00879	.00823	.00774	.00729
40	.0101	.00994	.00968	.00907	.00900	.00869	.00815	.00768	.00724
41	.00993	.00975	.00951	.00892	.00887	.00859	.00806	.00761	.00719
42	.00971	.00955	.00934	.00877	.00875	.00849	.00798	.00754	.00714
43	.00955	.00936	.00916	.00862	.00862	.00838	.00789	.00747	.00709
44	.00949	.00916	.00899	.00847	.00849	.00828	.00780	.00740	.00703
45	.00928	.00897	.00883	.00862	.00837	.00817	.00771	.00733	.00698
46	.00907	.00879	.00866	.00847	.00824	.00806	.00762	.00726	.00692
47	.00886	.00860	.00849	.00833	.00811	.00795	.00753	.00718	.00686
48	.00866	.00860	.00833	.00818	.00811	.00785	.00744	.00711	.00680
49	.00846	.00842	.00833	.00818	.00798	.00774	.00744	.00711	.00674

- 175 -

Table X-1-G (Continued). Leukemia, All Types Except CLL: Temporal Distribution T(A₁,Y) by Year Y After Exposure at Age A₁

A_1

Y	63	64	65	66	67	68	69	70	71
0	0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0	0
2	.00467	.00467	.00467	.00467	.00467	.00467	.00467	.00467	.00467
3	.0123	.0123	.0123	.0123	.0123	.0123	.0123	.0123	.0123
4	.0148	.0148	.0148	.0148	.0148	.0148	.0148	.0148	.0148
5	.0151	.0151	.0151	.0151	.0151	.0151	.0151	.0151	.0151
6	.0147	.0146	.0146	.0146	.0146	.0146	.0146	.0146	.0146
7	.0139	.0139	.0138	.0138	.0138	.0138	.0138	.0138	.0138
8	.0131	.0130	.0130	.0130	.0129	.0129	.0129	.0129	.0129
9	.0123	.0122	.0121	.0121	.0121	.0120	.0120	.0120	.0120
10	.0116	.0115	.0114	.0113	.0112	.0112	.0112	.0111	.0111
11	.0109	.0108	.0106	.0106	.0105	.0104	.0104	.0104	.0103
12	.0104	.0102	.0100	.00990	.00980	.00973	.00968	.00964	.00961
13	.00986	.00964	.00945	.00931	.00920	.00911	.00904	.00899	.00896
14	.00944	.00918	.00896	.00879	.00866	.00855	.00847	.00841	.00836
15	.00907	.00878	.00854	.00834	.00818	.00805	.00796	.00788	.00782
16	.00876	.00844	.00816	.00794	.00776	.00761	.00750	.00741	.00734
17	.00850	.00814	.00784	.00759	.00738	.00722	.00709	.00699	.00691
18	.00827	.00789	.00756	.00728	.00706	.00687	.00672	.00661	.00652
19	.00808	.00767	.00731	.00702	.00677	.00656	.00640	.00627	.00616
20	.00792	.00748	.00710	.00678	.00651	.00629	.00611	.00596	.00585
21	.00778	.00732	.00692	.00658	.00629	.00605	.00585	.00569	.00556
22	.00764	.00718	.00676	.00640	.00610	.00584	.00562	.00545	.00531
23	.00756	.00706	.00663	.00625	.00592	.00565	.00542	.00523	.00508
24	.00747	.00696	.00651	.00611	.00577	.00548	.00524	.00504	.00487
25	.00739	.00687	.00641	.00600	.00564	.00534	.00508	.00486	.00469
26	.00732	.00680	.00632	.00590	.00553	.00521	.00493	.00471	.00452
27	.00726	.00673	.00624	.00581	.00542	.00509	.00481	.00457	.00437
28	.00721	.00667	.00617	.00573	.00533	.00499	.00469	.00444	.00423
29	.00716	.00662	.00611	.00566	.00525	.00490	.00459	.00433	.00411
30	.00712	.00657	.00606	.00560	.00519	.00482	.00450	.00423	.00400
31	.00708	.00653	.00602	.00555	.00513	.00475	.00443	.00414	.00390
32	.00704	.00649	.00597	.00550	.00507	.00469	.00436	.00406	.00382
33	.00700	.00645	.00594	.00546	.00503	.00464	.00429	.00399	.00374
34	.00696	.00642	.00590	.00542	.00499	.00459	.00424	.00393	.00366
35	.00692	.00638	.00587	.00539	.00495	.00455	.00419	.00387	.00360
36	.00689	.00635	.00584	.00536	.00492	.00451	.00415	.00382	.00354
37	.00685	.00632	.00581	.00533	.00489	.00448	.00411	.00378	.00349
38	.00681	.00629	.00579	.00531	.00486	.00445	.00407	.00374	.00345
39	.00677	.00626	.00576	.00529	.00484	.00442	.00404	.00370	.00341
40	.00676	.00623	.00574	.00526	.00482	.00440	.00402	.00367	.00337
41	.00666	.00620	.00571	.00524	.00480	.00438	.00399	.00365	.00334
42	.00661	.00617	.00569	.00522	.00478	.00436	.00397	.00362	.00331
43	.00657	.00614	.00566	.00520	.00476	.00434	.00395	.00360	.00328
44	.00653	.00611	.00564	.00518	.00474	.00433	.00392	.00358	.00326
45	.00649	.00607	.00562	.00516	.00473	.00431	.00391	.00355	.00324
46	.00644	.00604	.00559	.00514	.00471	.00430	.00390	.00353	.00322
47	.00640	.00601	.00556	.00513	.00469	.00428	.00388	.00352	.00320
48	.00635	.00597	.00554	.00511	.00468	.00427	.00387	.00351	.00319
49	.00631	.00594	.00551	.00509	.00467	.00426	.00387	.00351	.00318

Table X-1-0 (Continued). Leukemia, All Types Except CLL: Temporal Distribution $T(A_1,Y)$ by Year Y After Exposure at Age A_1

Y	A_1			
	72	73	74	75
0	0	0	0	0
1	0	0	0	0
2	.00467	.00467	.00467	.00467
3	.0123	.0123	.0123	.0123
4	.0148	.0148	.0148	.0148
5	.0151	.0151	.0151	.0151
6	.0146	.0146	.0146	.0146
7	.0138	.0138	.0138	.0138
8	.0129	.0129	.0129	.0129
9	.0120	.0120	.0120	.0120
10	.0111	.0111	.0111	.0111
11	.0103	.0103	.0103	.0103
12	.00959	.00958	.00957	.00956
13	.00893	.00891	.00890	.00889
14	.00833	.00830	.00828	.00827
15	.00778	.00775	.00773	.00771
16	.00728	.00725	.00723	.00721
17	.00685	.00680	.00677	.00675
18	.00645	.00639	.00636	.00633
19	.00609	.00603	.00598	.00595
20	.00574	.00569	.00564	.00560
21	.00547	.00539	.00533	.00529
22	.00520	.00511	.00505	.00500
23	.00496	.00486	.00479	.00474
24	.00474	.00464	.00456	.00450
25	.00454	.00443	.00434	.00428
26	.00437	.00425	.00415	.00408
27	.00421	.00408	.00397	.00389
28	.00406	.00392	.00381	.00373
29	.00393	.00378	.00366	.00357
30	.00381	.00365	.00353	.00343
31	.00370	.00354	.00341	.00330
32	.00361	.00343	.00329	.00318
33	.00352	.00334	.00319	.00307
34	.00344	.00325	.00310	.00297
35	.00337	.00318	.00301	.00288
36	.00330	.00310	.00293	.00280
37	.00325	.00304	.00286	.00272
38	.00319	.00298	.00280	.00265
39	.00315	.00292	.00274	.00258
40	.00310	.00288	.00268	.00252
41	.00307	.00283	.00263	.00247
42	.00303	.00279	.00259	.00242
43	.00300	.00276	.00255	.00237
44	.00297	.00273	.00251	.00233
45	.00295	.00270	.00248	.00229
46	.00293	.00267	.00245	.00226
47	.00291	.00265	.00242	.00223
48	.00289	.00263	.00240	.00220
49	.00288	.00261	.00237	.00217

Table X-1-H. Leukemia, All Types Except CLL: Risk
Coefficient $E(A_1,S)$ by Exposure Age A_1 and Sex S

A_1	Sex		A_1	Sex	
	Male	Female		Male	Female
0	7.31	4.66	38	3.39	2.17
1	6.87	4.38	39	3.54	2.27
2	6.42	4.10	40	3.72	2.38
3	5.97	3.81	41	3.92	2.50
4	5.53	3.53	42	4.14	2.64
5	5.09	3.25	43	4.39	2.80
6	4.67	2.99	44	4.67	2.97
7	4.27	2.73	45	4.98	3.16
8	3.90	2.50	46	5.32	3.37
9	3.56	2.28	47	5.71	3.61
10	3.26	2.09	48	6.13	3.86
11	3.00	1.92	49	6.60	4.15
12	2.79	1.78	50	7.11	4.46
13	2.62	1.68	51	7.67	4.80
14	2.52	1.61	52	8.27	5.17
15	2.46	1.57	53	8.92	5.57
16	2.42	1.55	54	9.61	6.00
17	2.39	1.53	55	10.3	6.45
18	2.36	1.51	56	11.1	6.93
19	2.34	1.50	57	11.9	7.42
20	2.33	1.49	58	12.6	7.92
21	2.33	1.49	59	13.4	8.42
22	2.33	1.49	60	14.2	8.92
23	2.34	1.50	61	14.9	9.40
24	2.36	1.51	62	15.6	9.86
25	2.39	1.53	63	16.2	10.3
26	2.43	1.55	64	16.8	10.7
27	2.47	1.58	65	17.3	11.0
28	2.52	1.61	66	17.8	11.3
29	2.58	1.65	67	18.2	11.6
30	2.63	1.68	68	18.5	11.9
31	2.70	1.73	69	18.9	12.1
32	2.77	1.77	70	19.2	12.2
33	2.84	1.82	71	19.5	12.4
34	2.93	1.88	72	19.7	12.5
35	3.02	1.94	73	20.0	12.7
36	3.13	2.01	74	20.2	12.8
37	3.25	2.08	75	20.5	12.9

Table X-1-I. Leukemia, All Types Except CLL: Baseline Incidence I(λ_2,S) by Age at Diagnosis λ_2 and Sex S

λ_2	Sex		λ_2	Sex	
	Male	Female		Male	Female
0	7.00	5.70	43	4.22	3.47
1	7.00	5.70	44	4.52	3.70
2	7.00	5.70	45	4.87	3.97
3	6.65	5.44	46	5.24	4.25
4	5.83	4.80	47	5.60	4.50
5	4.80	4.01	48	5.98	4.73
6	3.86	3.27	49	6.38	4.95
7	3.30	2.80	50	6.80	5.16
8	3.04	2.54	51	7.25	5.38
9	2.81	2.31	52	7.71	5.60
10	2.64	2.10	53	8.20	5.85
11	2.54	1.93	54	8.77	6.15
12	2.50	1.80	55	9.47	6.51
13	2.53	1.68	56	10.3	6.92
14	2.58	1.56	57	11.4	7.41
15	2.65	1.46	58	12.7	7.97
16	2.69	1.40	59	14.0	8.60
17	2.70	1.40	60	15.3	9.29
18	2.63	1.44	61	16.7	10.0
19	2.49	1.48	62	18.0	10.7
20	2.34	1.52	63	19.2	11.5
21	2.23	1.56	64	20.4	12.2
22	2.20	1.60	65	21.6	13.0
23	2.29	1.64	66	22.9	13.8
24	2.45	1.68	67	24.2	14.6
25	2.64	1.72	68	26.2	15.5
26	2.80	1.76	69	28.9	16.6
27	2.90	1.80	70	32.3	17.7
28	2.93	1.84	71	35.9	18.9
29	2.94	1.88	72	39.6	20.2
30	2.94	1.93	73	43.3	21.6
31	2.96	2.00	74	47.1	23.3
32	3.00	2.10	75	50.9	25.1
33	3.07	2.22	76	54.8	27.0
34	3.15	2.34	77	58.6	29.0
35	3.23	2.46	78	62.8	31.5
36	3.31	2.58	79	67.2	34.5
37	3.40	2.70	80	71.6	37.5
38	3.49	2.82	81	75.8	40.2
39	3.59	2.94	82	79.4	42.1
40	3.71	3.06	83	82.1	43.5
41	3.84	3.18	84	84.0	44.6
42	4.00	3.30	85	85.3	45.5

2. Cancer of Bones and Joints (170 in ICDA-8)

Bone cancer is relatively uncommon and radiogenic bone cancer has been seen mainly in association with internally deposited isotopes of radium, especially in radium-dial painters exposed to long-lived radium-226 and -228 (10), and in German patients treated with short-lived radium-224 for tuberculosis and ankylosing spondylitis (11). Radiogenic bone cancer has also been reported following high doses of X rays (4), especially among ankylosing spondylitis patients. It has not been seen in the A-bomb survivors (4).

For the BEIR III report, risk coefficients were first calculated for repeated acute exposures to radium-224 and the "provisional" low-LET coefficients, as they are termed in the BEIR report, were derived from them through the use of the ICRP quality factor of 20 for alpha particles. Tables were prepared for leukemia plus bone cancer and not for each separately. This was done because the temporal distribution of excess bone cancer is rather like that for leukemia: the latent period is short, four years or less, and the total period of expression, perhaps 20-25 years.

Since the only human data on the risk of bone cancer following exposure to low-LET radiation pertain to therapeutic levels of dose, the Working Group decided that it should not make PC estimates for bone cancer resulting from low-LET radiation but should confine its calculations to the alpha radiation on which the BEIR estimates rest. The BEIR III linear estimate, based on the radium-224 experience, is one excess bone cancer per million persons per year per rad of alpha radiation to endosteal tissue (4). Hence Table X-2-B will not be used for the purpose of PC estimation for exposure to low-LET radiation, or to greatly protracted high-LET radiation from, e.g., radium-226.

The BEIR report provides little basis for a choice for either the dose-response or the time-response model. The linear function is assumed for high-LET radiation, but more for consistency with experimental results for tumors generally rather than because of the empirical evidence on the induction of bone cancer in man following exposure to radium-224. For alpha particles from radium-224 the BEIR risk coefficient of 1 per million persons per year per rad of endosteal dose is a fairly stable linear estimate, being based on 54 cases vs. an expectation of only 0.2 cases (11). Information on variation with age is only fair, but the indications are that younger patients experienced a risk very little higher than that of adult patients, and no sex differential was observed (4). The lowest doses at which excess cases have been observed in the radium-224 series are above 50 rad of alpha radiation to the endosteum, so that the applicability of the data to lower doses remains uncertain. The best PC estimates would be those for doses of radium-224 alpha radiation within the observed range, average skeletal doses being mostly above 90 rad.

The BEIR committee employed a constant absolute risk (plateau) for bone cancer in combining it with leukemia, with no dose threshold, but the Working Group has used a wave function, as it has for leukemia, and for this assumption there is good recent evidence (12). Published data from the German radium-224 series were used to fit a lognormal induction

period model (13). The fitted model had a minimum induction period of 1.52 years and the natural logarithm of time after the minimum had a mean of 2.12 and a variance of 0.48.

United States incidence data for cancers of bones and joints have been taken from the SEER data bank for 1973-1981 (8). As may be seen from Tables VII-1 and VII-2, there is relatively little variation among the SEER reporting areas (8), although a sex differential is well established, females having about 60 percent of the level reported for males. Radiation is the only environmental factor that is known to play an etiologic role in bone cancer (14). Statistical studies of racial differences in the incidence of Ewing's tumor and studies of family aggregations point to the influence of genetic factors on some forms of bone cancer (15). If an individual is known to be a member of a sub-population with an elevated baseline risk, then the PC estimate obtained on the basis of the SEER rates will be excessive (see Chapter IV-G and Chapter IX).

For bone cancer, as for leukemia, the relative excess, R, in the basic equation

$$PC = R/(1 + R)$$

is found as the product of three functions, i.e.,

$$R = F \times T \times K$$

where $F = F(D)$ represents the alpha radiation dose to endosteal tissue (D); $T = T(Y)$ represents the influence of the interval from exposure to diagnosis; and $K = K(A_1, A_2, S)$ represents relative excess of bone cancer for a person of sex S and ages A_1 and A_2 at exposure and diagnosis, respectively, when both F and T = 1. Here K is found as

$$K = E(A_1, S)/I(A_2, S)$$

where $E(A_1, S)$ is derived from BEIR III and is an estimate of the probability that a radiation-induced bone cancer will be diagnosed at some time after exposure to radium-224, and is expressed in units of dose. For each exposure age A_1 and sex S, $E(A_1, S)$ was determined such that the average of $E(A_1, S) \times T(Y)$ over the BEIR III plateau period (Y = 2 through 28) was equal to the BEIR coefficient, 0.1 excess cancers per hundred thousand persons per year per rad.

Look-up tables are provided below for the following coefficients:

$T(Y)$, Table X-2-A;

$E(A_1, S)$, Table X-2-B;

$I(A_2, S)$, Table X-2-C.

Here, under the linear model assumed for high-LET radiation, the endosteal dose in rad is

$$F = D.$$

The constant relative risk model for time to response was not assumed to hold for bone cancer, which appears to follow a "wave" function, and therefore the factor T is the probability that a cancer caused by an exposure at age A_1 will be diagnosed Y years later.

A few examples are given below to illustrate the use of the tables in deriving the PC values.

Example #1   A typical male, exposed to 50 rad of brief alpha radiation to endosteal tissue at age 10, with a diagnosis of bone cancer 6.5 years later, at age 16. Then $A_1 = 10$, $A_2 = 16$, $Y = 6$, and $D = 50$

$$F(D) = 50$$

$$T(Y) = T(6) = .0874$$

$$E(A_1,S) = E(10,m) = 2.79$$

$$I(A_2,S) = I(16,m) = 1.54$$

$$K = E/I = 2.79/1.54 = 1.812$$

then $R = F \times T \times K = 50 \times .0874 \times 1.812 = 7.91$

and $PC = R/(1 + R) = 7.91/8.91 = .89$ or 89%.

Example #2   A typical female exposed to 100 rad of brief alpha radiation to endosteal tissue at age 7, with a diagnosis of bone cancer at age 20, 12.5 years after exposure. Then $A_1 = 7$, $A_2 = 20$, $Y = 12$, and $D = 100$.

$$F(D) = 100$$

$$T(12) = .0485$$

$$E(7,f) = 2.81$$

$$I(20,f) = .781$$

$$K = E/I = 2.81/.781 = 3.60$$

then $R = F \times T \times K = 100 \times .0485 \times 3.60 = 17.5$

and $PC = R/(1+R) = 17.5/18.5 = .946$ or 95%.

The uncertainty surrounding PC estimates is discussed in Chapter VII, and Section VII-0 includes a derivation of approximate 90 percent credibility intervals for PC estimates.

To provide some orientation to the general magnitude of the PC values resulting from the procedures described here for bone cancer, Fig. X-2 has been drawn for endosteal doses of 1, 10, and 100 rad to show the PC values by age at exposure and sex. The figure is in 8 parts corresponding to ages 0, 10, 20, 30, 40, 50, 60, and 70 at exposure. The vertical scale is logarithmic and curves are presented for only three radiation dose levels. For these and other reasons interpolation is to be discouraged.

- 182 -

Fig X-2-1

BONE AND JOINT CANCER*
EXPOSURE AGE 0
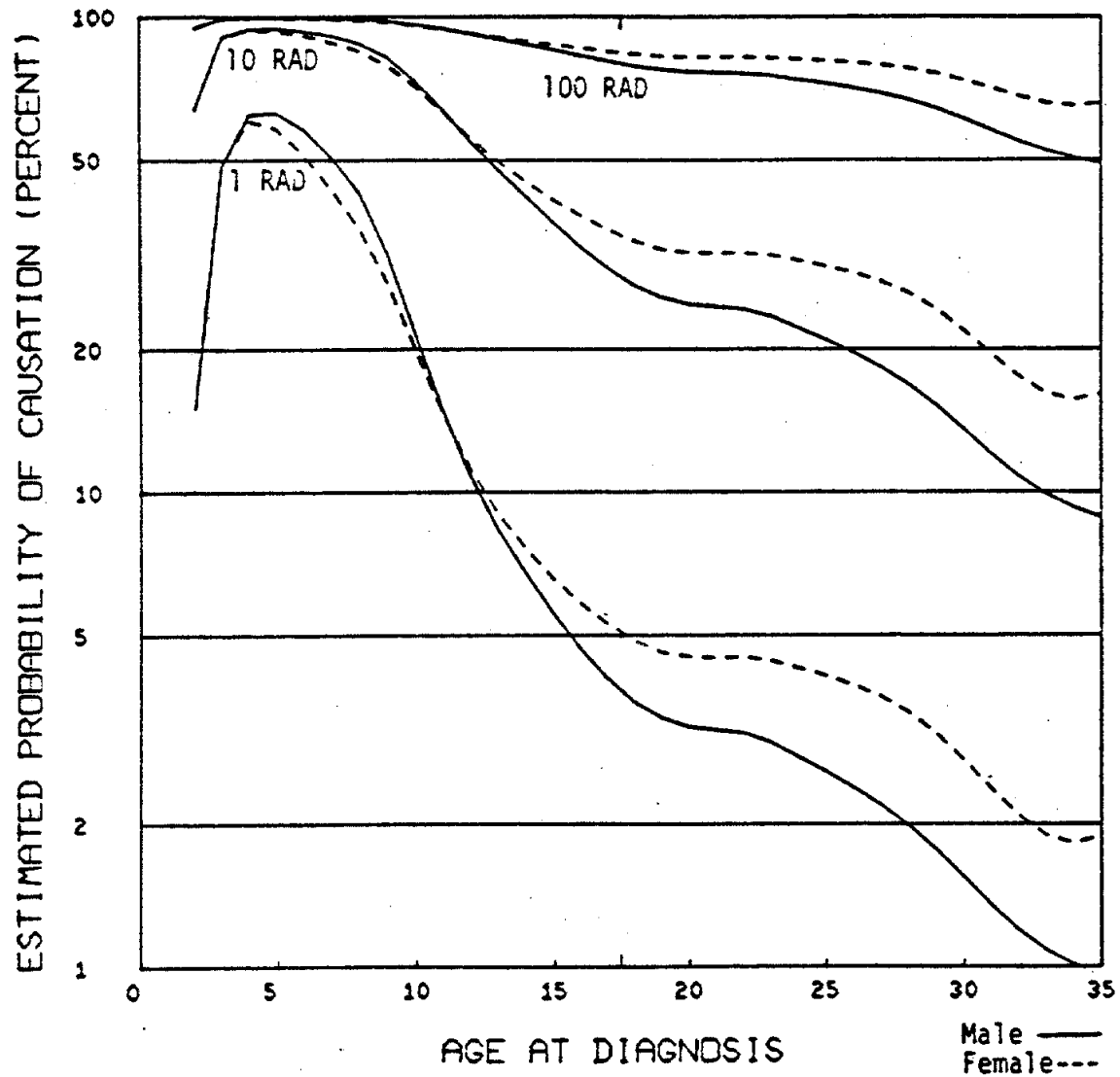
*Alpha radiation from radium-224 only

Fig X-2-2

BONE AND JOINT CANCER*
EXPOSURE AGE 10
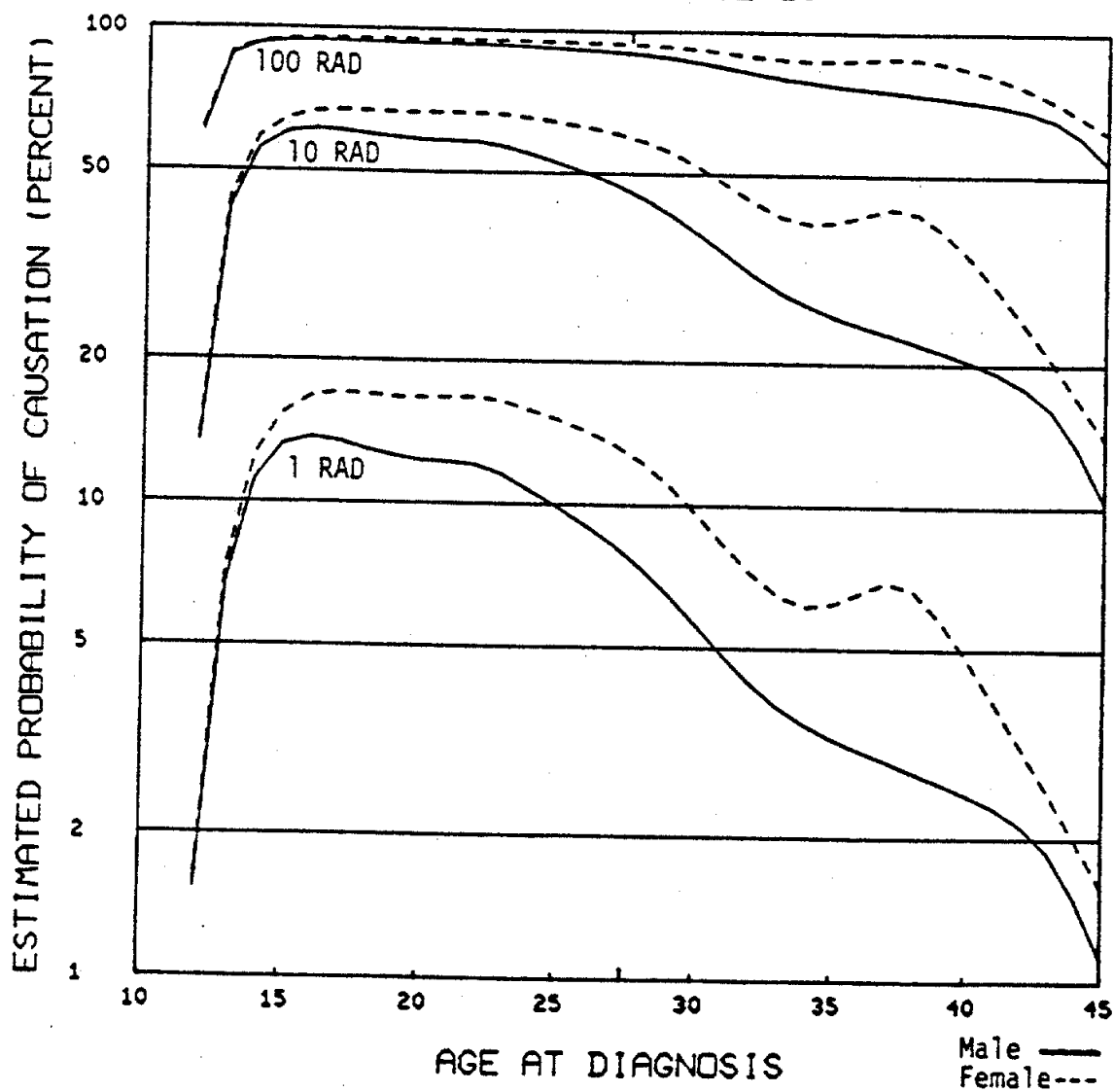
*Alpha radiation from radium-224 only

Fig X-2-3

BONE AND JOINT CANCER *
EXPOSURE AGE 20
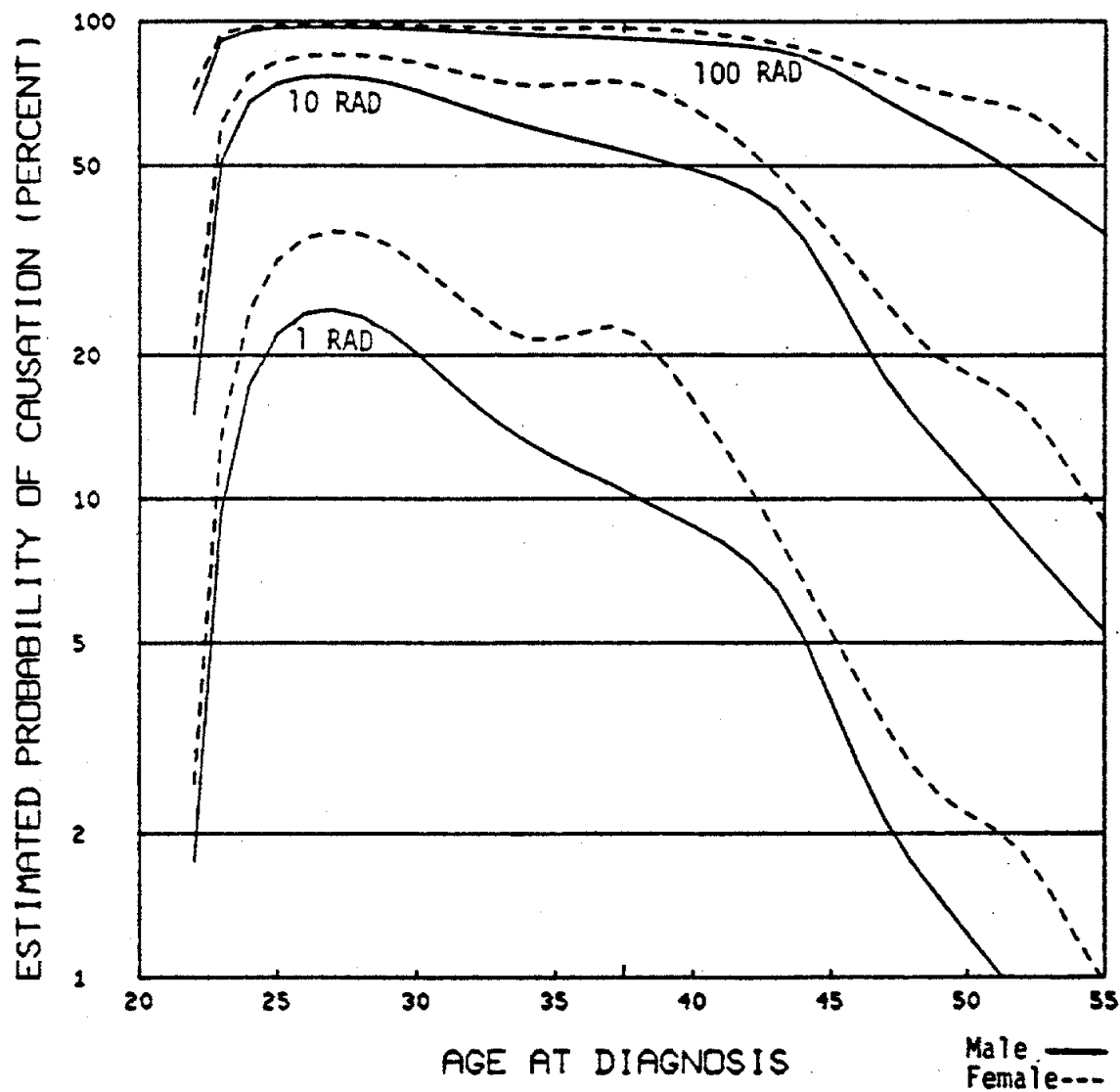
*Alpha radiation from radium-224 only

Fig X-2-4

BONE AND JOINT CANCER*
EXPOSURE AGE 30

*Alpha radiation from radium-224 only

- 186 -
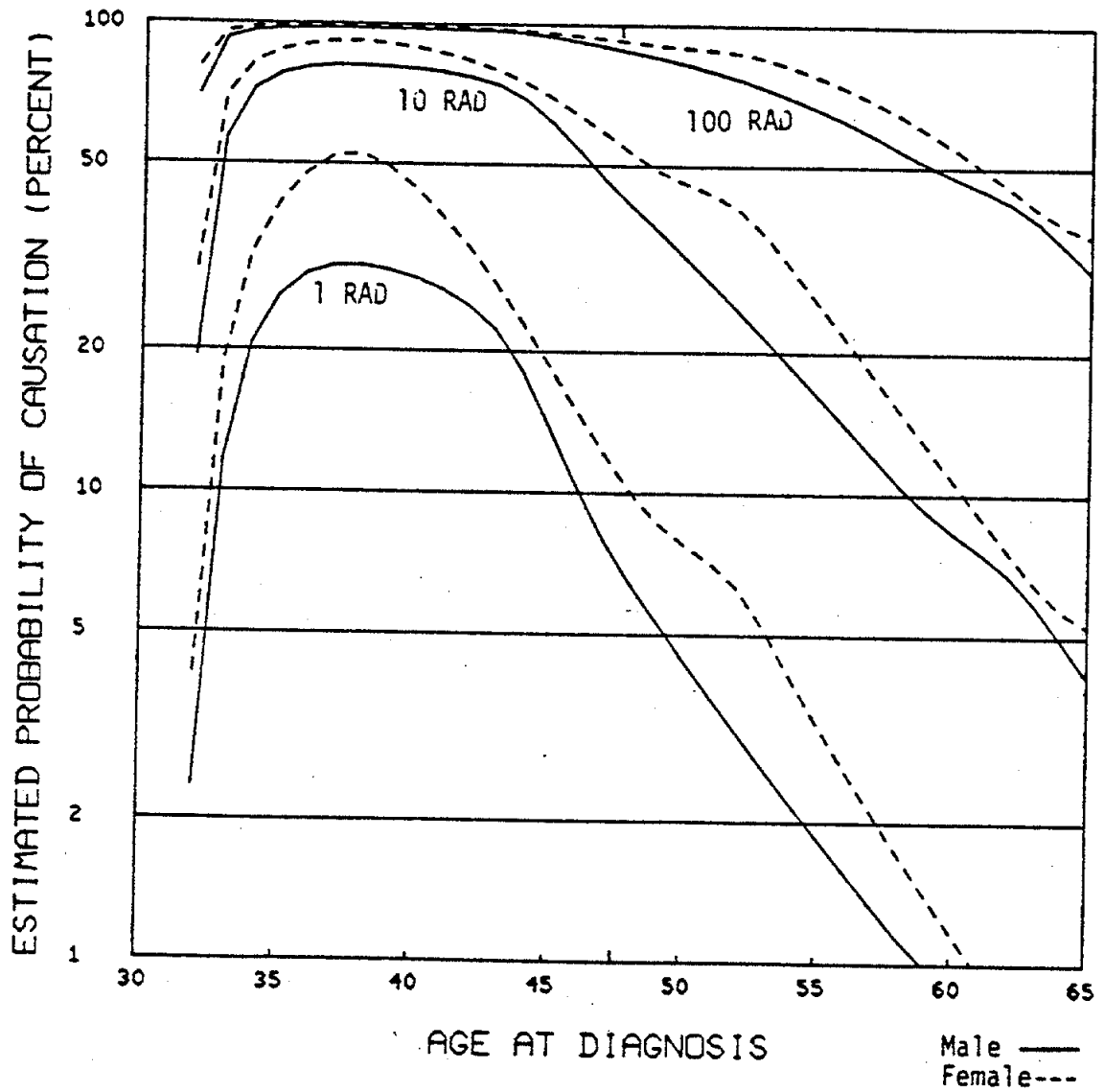
Fig X-2-5

BONE AND JOINT CANCER *
EXPOSURE AGE 40

*Alpha radiation from radium-224 only
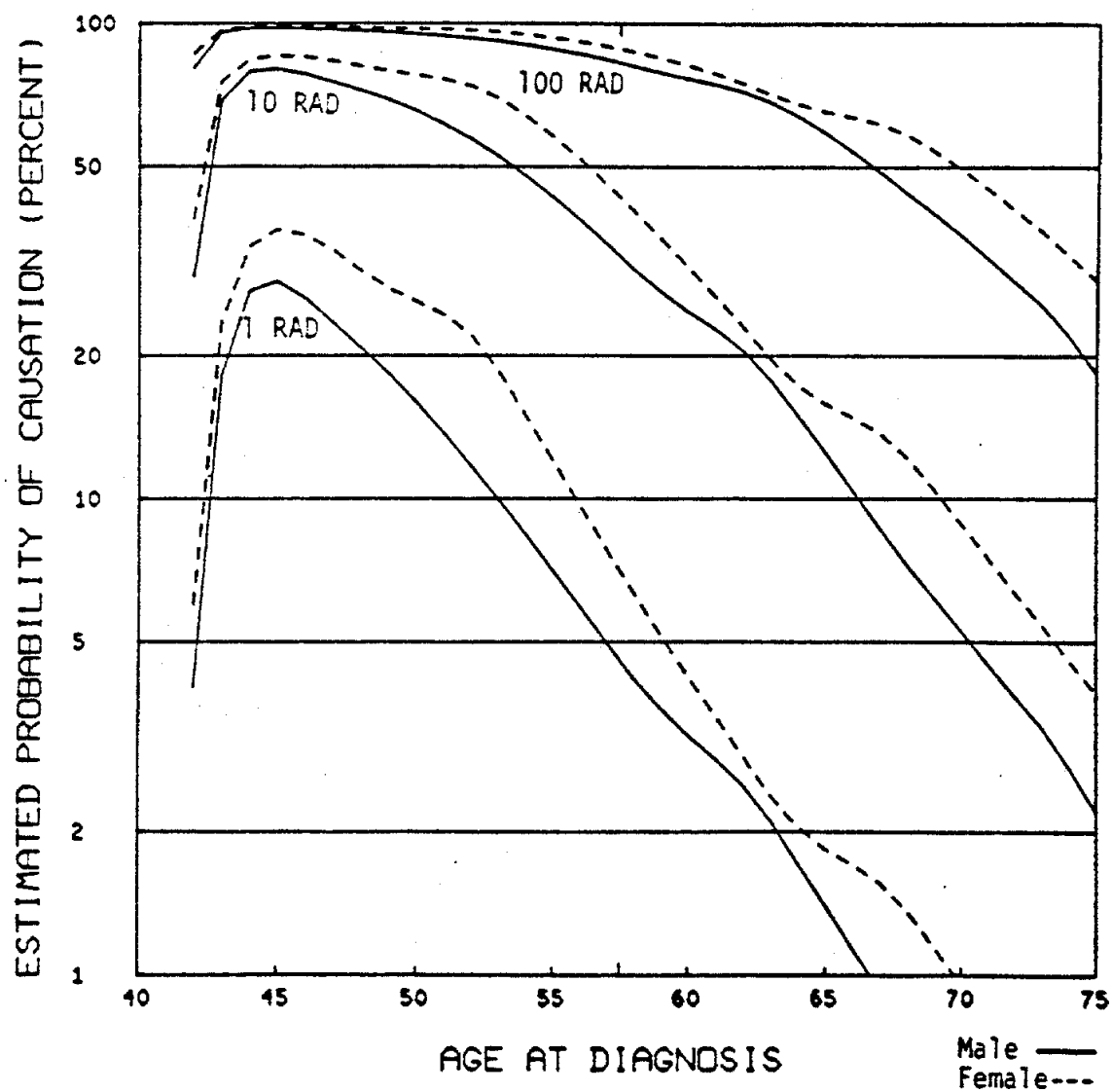
Fig X-2-6

BONE AND JOINT CANCER*
EXPOSURE AGE 50
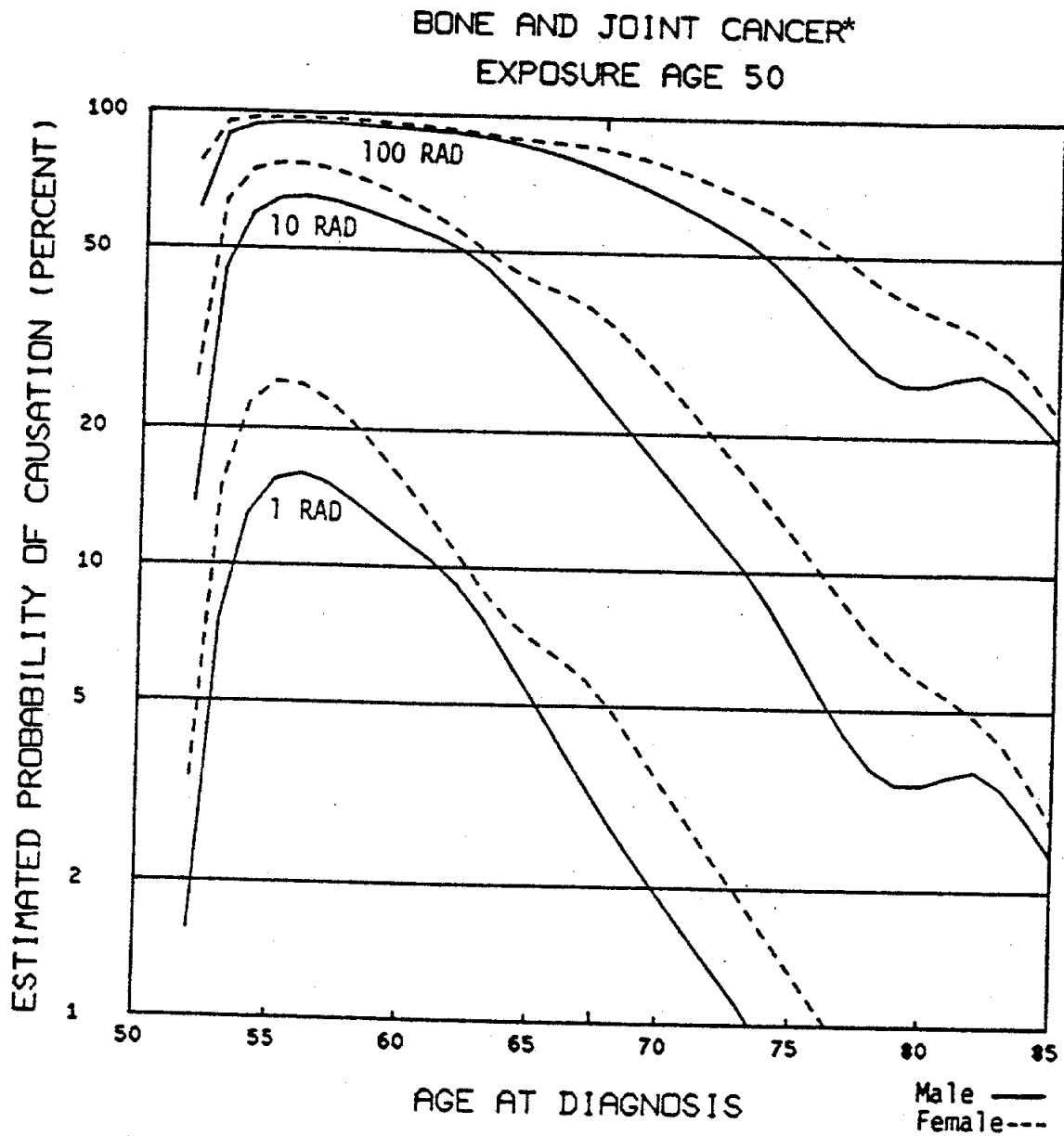
*Alpha radiation from radium-224 only

Fig X-2-7

BONE AND JOINT CANCER*
EXPOSURE AGE 60

*Alpha radiation from radium-224 only

Fig X-2-8

BONE AND JOINT CANCER*
EXPOSURE AGE 70
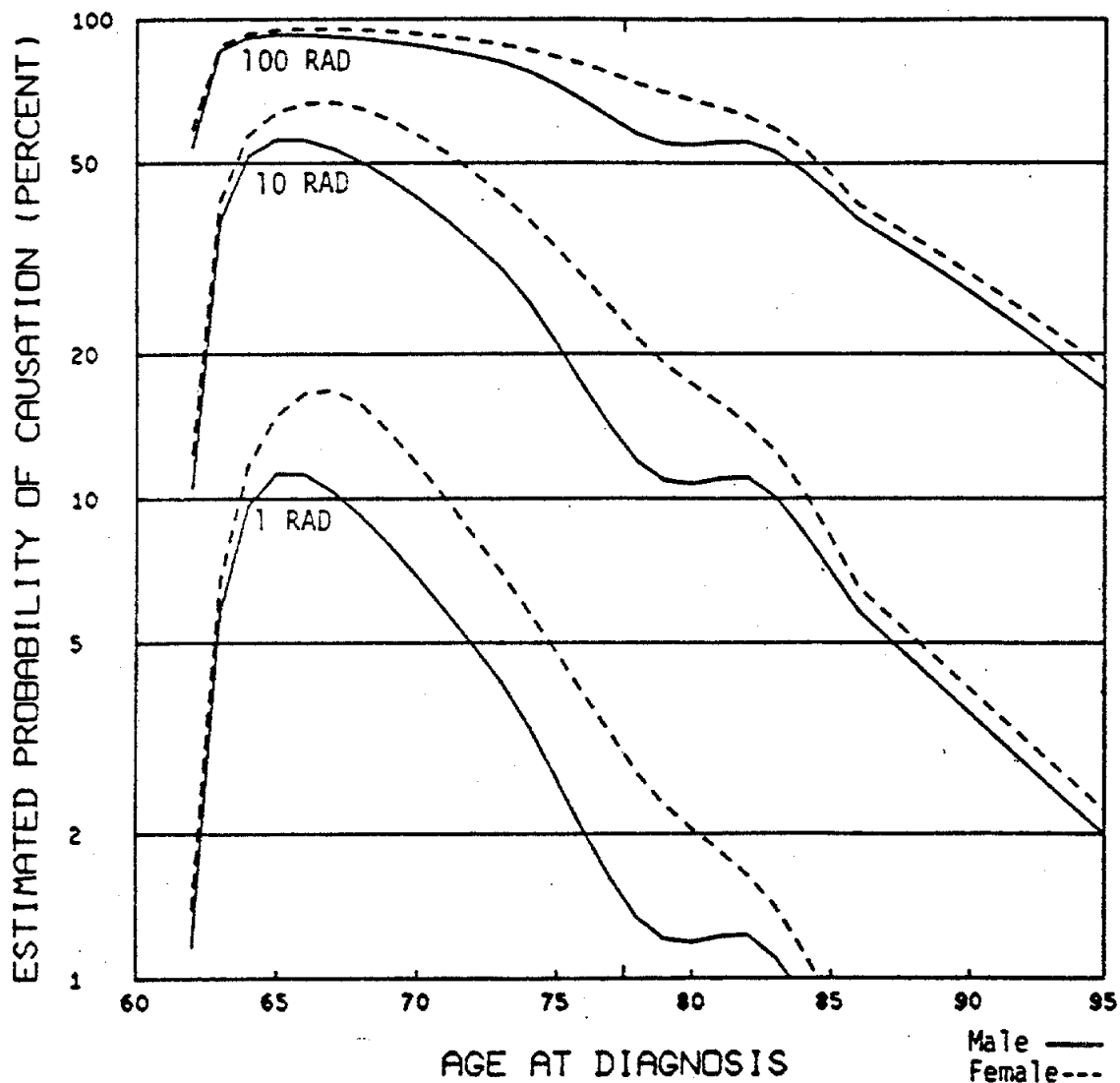
*Alpha radiation from radium-224 only
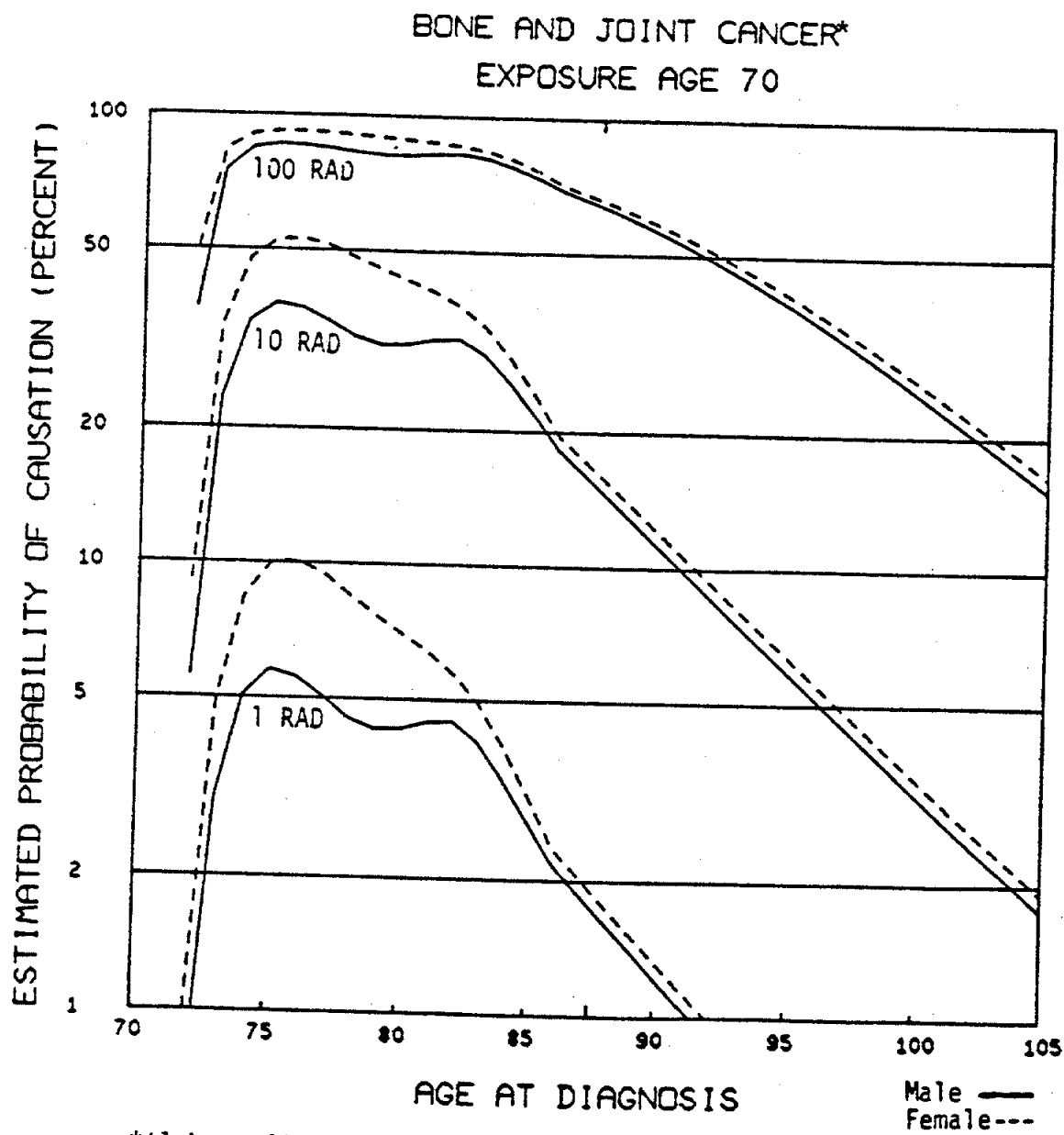
Table X-2-A. Bone and Joint Cancer:
  Temporal Distribution T(Y) by Year Y
  After Exposure

Y	T(Y)	Y	T(Y)
0	0	25	.00750
1	.0000190	26	.00657
2	.00629	27	.00577
3	.0338	28	.00507
4	.0637	29	.00446
5	.0814	30	.00394
6	.0874	31	.00348
7	.0857	32	.00308
8	.0798	33	.00274
9	.0720	34	.00243
10	.0638	35	.00216
11	.0558	36	.00193
12	.0485	37	.00172
13	.0419	38	.00154
14	.0362	39	.00138
15	.0312	40	.00124
16	.0269	41	.00111
17	.0232	42	.00100
18	.0200	43	.000900
19	.0173	44	.000812
20	.0150	45	.000733
21	.0130	46	.000662
22	.0113	47	.000600
23	.00984	48	.000543
24	.00858	49	.000493

Table X-2-B. Bone and Joint Cancer: Risk Coefficient E(A₁,S) by Exposure Age A₁ and Sex S

A_1	Male	Female	A_1	Male	Female
0	2.80	2.81	38	2.65	2.73
1	2.80	2.81	39	2.63	2.72
2	2.80	2.81	40	2.62	2.71
3	2.80	2.81	41	2.60	2.71
4	2.80	2.81	42	2.59	2.70
5	2.80	2.81	43	2.57	2.69
6	2.80	2.81	44	2.55	2.68
7	2.79	2.81	45	2.53	2.67
8	2.79	2.81	46	2.51	2.65
9	2.79	2.81	47	2.49	2.64
10	2.79	2.81	48	2.47	2.63
11	2.79	2.81	49	2.45	2.61
12	2.79	2.81	50	2.42	2.59
13	2.79	2.81	51	2.40	2.58
14	2.79	2.81	52	2.37	2.55
15	2.79	2.80	53	2.35	2.53
16	2.79	2.80	54	2.32	2.51
17	2.79	2.80	55	2.30	2.48
18	2.78	2.80	56	2.27	2.46
19	2.78	2.80	57	2.24	2.43
20	2.78	2.80	58	2.21	2.40
21	2.78	2.80	59	2.18	2.37
22	2.77	2.79	60	2.16	2.33
23	2.77	2.79	61	2.13	2.30
24	2.77	2.79	62	2.10	2.26
25	2.76	2.79	63	2.07	2.23
26	2.76	2.78	64	2.04	2.19
27	2.75	2.78	65	2.02	2.15
28	2.74	2.78	66	1.99	2.12
29	2.74	2.77	67	1.97	2.08
30	2.73	2.77	68	1.95	2.05
31	2.72	2.77	69	1.92	2.02
32	2.71	2.76	70	1.91	1.98
33	2.71	2.76	71	1.89	1.96
34	2.70	2.75	72	1.87	1.93
35	2.68	2.75	73	1.86	1.90
36	2.67	2.74	74	1.85	1.88
37	2.66	2.74	75	1.84	1.86

Table X-2-C. Bone and Joint Cancer: Baseline Incidence $I(\lambda_2,S)$ by Age at Diagnosis λ_2 and Sex S

λ_2	Sex		λ_2	Sex	
	Male	Female		Male	Female
0	.100	.100	43	.444	.337
1	.100	.100	44	.532	.379
2	.100	.100	45	.638	.424
3	.109	.118	46	.736	.465
4	.136	.165	47	.801	.500
5	.178	.234	48	.841	.510
6	.233	.315	49	.881	.493
7	.300	.400	50	.921	.471
8	.431	.528	51	.961	.467
9	.646	.714	52	1.00	.501
10	.896	.916	53	1.04	.561
11	1.13	1.09	54	1.08	.621
12	1.30	1.20	55	1.12	.681
13	1.41	1.24	56	1.16	.741
14	1.49	1.25	57	1.20	.801
15	1.54	1.22	58	1.21	.861
16	1.54	1.17	59	1.20	.921
17	1.50	1.10	60	1.17	.981
18	1.40	1.01	61	1.16	1.04
19	1.27	.895	62	1.20	1.10
20	1.12	.781	63	1.29	1.12
21	.987	.677	64	1.39	1.09
22	.900	.600	65	1.50	1.03
23	.845	.543	66	1.61	.991
24	.795	.494	67	1.71	1.00
25	.753	.453	68	1.79	1.05
26	.720	.421	69	1.87	1.11
27	.700	.400	70	1.95	1.17
28	.696	.392	71	2.03	1.24
29	.703	.396	72	2.11	1.30
30	.713	.404	73	2.28	1.38
31	.715	.408	74	2.54	1.46
32	.700	.400	75	2.83	1.55
33	.667	.369	76	3.07	1.63
34	.627	.318	77	3.21	1.71
35	.582	.263	78	3.07	1.72
36	.538	.218	79	2.71	1.68
37	.500	.200	80	2.29	1.62
38	.465	.205	81	1.97	1.59
39	.434	.220	82	1.91	1.61
40	.409	.242	83	2.00	1.74
41	.396	.269	84	2.15	1.95
42	.400	.300	85	2.31	2.21

3. Salivary Gland Cancer (142 in ICDA-8)

The 1980 BEIR report (4) included the salivary glands among the sites sensitive to radiation carcinogenesis, but probably only at high dose levels, and summary risk coefficients were not presented. The evidence for a radiation effect rests mainly on follow-up studies of patients with histories of therapeutic irradiation to the head and neck during infancy or childhood, with doses to the salivary gland ranging from about 40 rad for X-ray epilation of the scalp to as much as 800 rad for irradiation of the thymus gland or the tonsils (16-22). A recent review (23) included a linear regression analysis of dose response in which data from these studies were combined. The several studies agreed reasonably well with an estimated excess risk per rad of 0.26 cases per million person-years, when a minimal induction period of 5 years was assumed. Estimates also were derived from two studies of A-bomb survivors (24,25), but these estimates seemed less reliable because of limited data in one and uncertain dosimetry and uncertain numbers of person-years in the other.

The Working Group considers that available data support an estimated risk of 0.26 excess salivary gland cancers per million person-years per rad following a radiation exposure during infancy or childhood, that is, before age 15. This level of risk applies 10 years after exposure, with somewhat lower risks 5-9 years after exposure. No estimate was calculated for exposures at older ages.

The available data are much too fragile for critical examination of dose-response and time-response models appropriate to the salivary glands, and the Working Group has assumed that excess cancer of the salivary glands could be adequately described by means of the linear-quadratic dose-response model and the constant relative risk time-response model. The standard assumptions as to absence of threshold and 10-year latent period, smoothed as described in Chapter VI, have also been made.

Incidence data for the U.S. have been extracted from the data bank for the SEER program of the National Cancer Institute. The rates used to represent normal or baseline incidence are for the period 1973-1981, all races combined, and all reporting areas combined except Puerto Rico. There is little variation among the reporting areas as to level of risk, but the rates for females are about 75 percent of those for males (8).

As noted in Chapter IV-G and in Chapter IX, risk factors other than ionizing radiation may be taken into consideration in interpreting the PC values derived by the procedures presented here. If it is believed that some other risk factor operates additively with radiation, and the individual is thought to have been exposed to that risk factor to an extent greater than the average for the population generally, then the PC obtained from the present procedures will be somewhat excessive. But if it is believed that the second risk factor may combine with radiation to enhance risk in multiplicative fashion, the PC estimates based on these procedures should be unbiassed.

The procedures for calculating PC values for cancers of the salivary glands based on the assumptions and principles of Chapter V and are detailed in Chapters VI and IX. For cancers of the salivary glands, as

for cancers of most other sites, the relative excess, R, in the basic equation

$$PC = R/(1 + R)$$

is found as the product of three functions, i.e.,

$$R = F(D) \times T(Y) \times K(A_1,S)$$

where $F(D)$ represents the tissue dose (D) in rad, $T(Y)$ the influence of the time from exposure to diagnosis (Y), and $K(A_1,S)$ the relative excess risk of salivary gland cancer for a person of age at exposure A_1 and sex S, when both F and T = 1.

Under the linear-quadratic model assumed for cancers of the salivary gland, when exposure is to low-LET radiation

$$F = D + D^2/116.$$

For cancers of the salivary glands, the influence of time, T, depends entirely upon completed years from exposure to diagnosis (Y). The function T is tabulated below.

Y	0-4	5	6	7	8	9	10+
T	0	.074	.259	.500	.741	.926	1

The standardized relative risk of excess cancer of the salivary glands, K, is given in the accompanying table for low-LET radiation and for each sex and year of age (completed years) from birth to age 14.

A few examples should clarify the actual computational procedures for cancers of the salivary glands following exposure to ionizing radiation.

Example #1   A typical female, exposed at age 5 to 3 rad of low-LET radiation to the salivary glands, with diagnosis at age 12, 7.2 years after exposure. Then D = 3, A_1 = 5, and Y = 7.

$$F(D) = 3 + 3^2/116 = 3.1$$

$$T(Y) = T(7) = 0.5$$

$$K(A_1,S) = K(5,f) = .0300$$

and R may be found from the relation

$$R = F \times T \times K = 3.1 \times 0.5 \times .030 = .0465$$

$$\text{and } PC = R/(1+R) = .0465/1.0465 = .044, \text{ or } 4\%.$$

Example #2   A typical male, exposed at age 18 to 5 rad of low-LET radiation to the salivary glands, with diagnosis at age 30. No estimate can be made because the information is not available for estimating the risk associated with exposure after age 14.

Example #3   A typical male, aged 7 at first exposure to 6 rad of low-LET radiation to the salivary glands, and aged 12 at the second exposure to 5 rad of low-LET radiation, with diagnosis at age 20, 8.3 years after the second exposure and more than 10 years after the first. This example requires that two estimates of R be made, one for each exposure.

Exposure at age 7, when $D = 6$, $A_1 = 7$, and $Y = 13$

$F(6) = 6 + 6^2/116 = 6.31$

$T(13) = 1$

$K(7,m) = .0311$

and $R(7) = F \times T \times K = 6.31 \times 1 \times .0311 = .196$

Exposure at age 12, when $D = 5$, $A_1 = 12$, and $Y = 8$

$F(5) = 5 + 5^2/116 = 5.22$

$T(8) = .741$

$K(12,m) = .0214$

$R(12) = 5.22 \times .741 \times .0214 = .0828$

then $R = R(7) + R(12) = .196 + .083 = .279$

and $PC = R/(1 + R) = .279/1.279 = .22$ or 22%.

The uncertainty surrounding PC estimates is discussed in Chapter VII and Section VII-0 includes a derivation of approximate 90 percent credibility intervals for PC estimates.

To provide some orientation to the general magnitude of the PC values resulting from the procedures described here for the salivary glands, Fig X-3 has been drawn for tissue doses of 1, 10, and 100 rad to show the PC values by age at exposure and sex. The calculations were performed with $T(Y) = 1$, i.e., on the assumption that the interval from exposure to diagnosis was 10 or more years. The vertical scale is logarithmic and curves are presented for only three radiation dose levels. For these and other reasons interpolation is to be discouraged.

Fig. X-3

SALIVARY GLAND CANCER
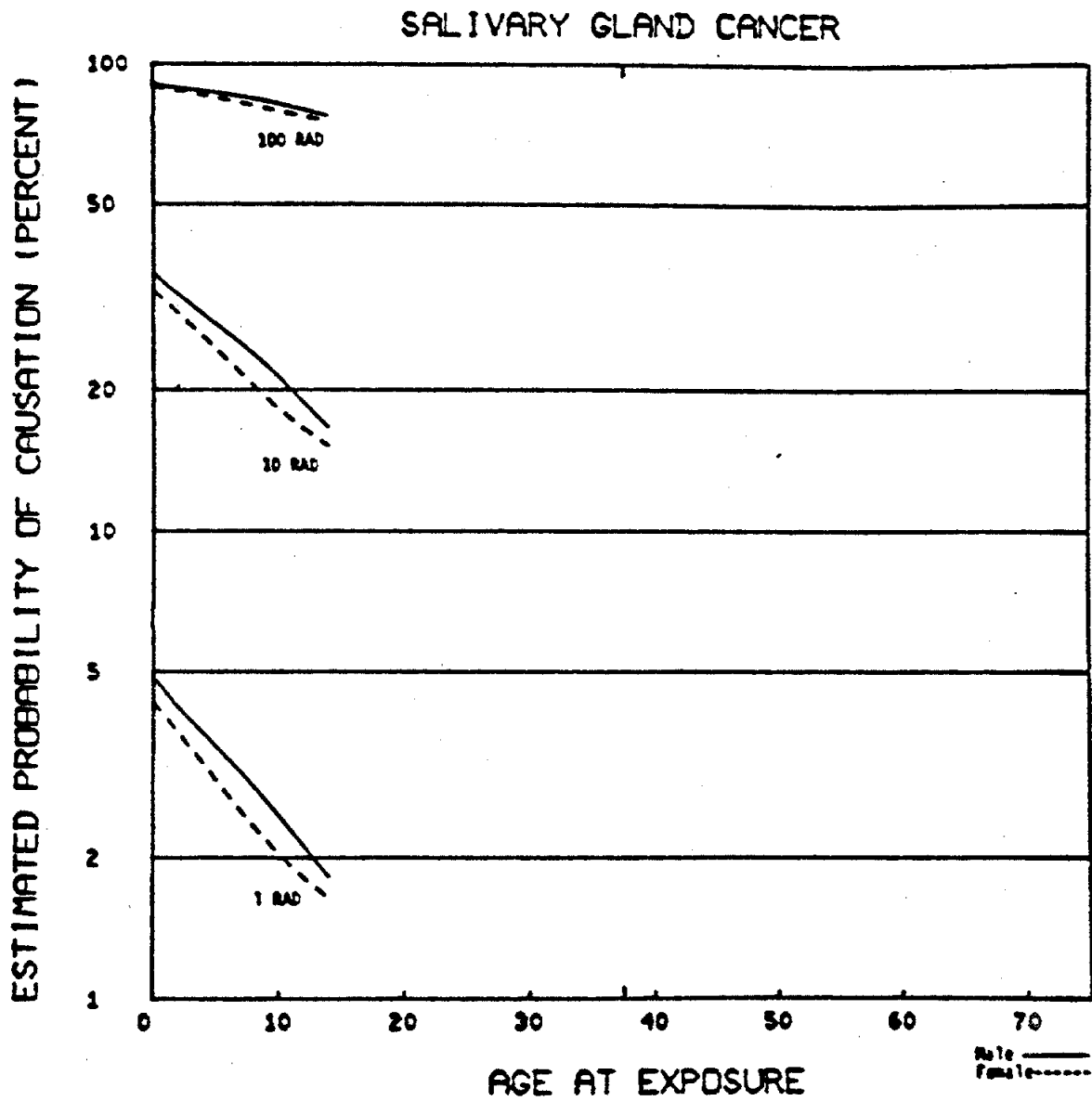
Table X-3.　Salivary Gland Cancer: Relative Excess
$K(A_1, S)$ by Exposure Age A_1 and Sex S

A_1	Sex		A_1	Sex	
	Male	Female		Male	Female
0	.0509	.0446	8	.0290	.0237
1	.0467	.0412	9	.0270	.0221
2	.0433	.0380	10	.0250	.0206
3	.0405	.0351	11	.0231	.0194
4	.0379	.0325	12	.0214	.0183
5	.0355	.0300	13	.0198	.0174
6	.0332	.0277	14	.0184	.0165
7	.0311	.0256			

4. Esophageal Cancer (150 in ICDA-8)

    The esophagus is apparently not especially sensitive to the carcino-
genic influence of ionizing radiation, but is included among the sites
for which risk estimates have been made by both the BEIR III committee
(4) and the UN committee in its 1977 report (2). The Working Group has
employed the BEIR III risk coefficients (adjusted to the period 11-30
years after exposure) for individuals exposed after age 20; those for
exposure under age 20 were considered unreliable for the present purpose
(see Chapter VII-F). The BEIR III committee relied heavily on both experi-
mental and human data in selecting the esophagus for inclusion among the
sites for which risk might be estimated. Human data, however, are rather
few and derive largely from the small series among the British ankylosing
spondylitis patients (26) and the larger series among A-bomb survivors
(27). The BEIR committee used the risk coefficients for fatal esophageal
cancer among the A-bomb survivors as its incidence estimates, since the
case-fatality of esophageal cancer is so very high. More recent reports
on the experience of the A-bomb survivors have not altered the evidence
of the relative sensitivity of esophageal tissue to the carcinogenic
action of radiation (28-30).

    Neither the dose-response nor the time-response characteristics of
radiation-induced esophageal cancer have been studied sufficiently to pro-
vide independent evidence as to the functions most suitable for this
site. The Working Group has chosen, therefore, to employ the linear-
quadratic dose-response function, with no threshold, and the constant
relative risk model to describe the distribution of excess cases over
time with a latent period of 10 years smoothed as described in Chapter
V-C.

    Estimates of baseline incidence are based on the SEER data bank of
the National Cancer Institute (8). The rates are for the period 1973-1981,
for all races combined, and for all reporting areas combined except
Puerto Rico. As noted in Chapter VII-C, Tables VII-1 and VII-2, there is
considerable variation among the SEER reporting areas with respect to the
incidence of esophageal cancer. The major risk factors that have been
identified are alcohol consumption and cigarette smoking (31). As noted
in Chapter IV-G and in Chapter IX, risk factors other than ionizing
radiation may be taken into consideration in interpreting the PC values
derived by the procedures presented here. If it is believed that some
other risk factor operates additively with radiation, and the individual
is thought to have been exposed to that risk factor to an extent greater
than the average for the population generally, then the PC obtained from
the present procedures will be somewhat excessive. But if it is believed
that the second risk factor may combine with radiation to enhance risk in
multiplicative fashion, the PC estimates based on these procedures should
be unbiassed. Day and Munoz (31) cite the data of Tuyns et al. (32) as
providing evidence that a multiplicative model fits well the combined
influence of alcohol consumption and smoking upon the risk of esophageal
cancer. There are, however, no good data bearing on the issue with
respect to ionizing radiation and no numerical adjustment is provided
here.

For esophageal cancer the relative excess, R, in the basic equation

$$PC = R/(1 + R)$$

is found as the product of three functions, i.e.,

$$R = F(D) \times T(Y) \times K(A_1,S)$$

where $F(D)$ represents the contribution of the tissue dose, $T(Y)$ represents the conditioning influence of years from exposure to diagnosis (Y), and $K(A_1,S)$ represents the relative excess risk of esophageal cancer for a person of sex S and age at exposure A_1, when both F and T = 1.

Under the linear-quadratic model assumed for esophageal cancer when exposure is to low-LET radiation

$$F = D + D^2/116$$

For the esophagus the influence of time (T) on the relative risk depends only on years from exposure to diagnosis (Y). The function T is tabulated below:

Y	0-4	5	6	7	8	9	10+
T	0	.074	.259	.500	.741	.926	1.

The standardized relative risk of excess esophageal cancer, K, is given in the accompanying Table X.4 for low-LET radiation and for each sex and year of age (completed years) from 20 to 75.

A few examples should make it clear how the PC values are to be calculated in individual cases:

Example 1   A male, exposed to 5 rad of low-LET radiation to the esophagus at age 20, with a diagnosis of esophageal cancer at age 50, otherwise typical of his age-sex classification with respect to the risk of esophageal cancer. Here D = 5, A_1 = 20, and Y = 30.

$$F(D) = 5 + 5^2/116 = 5.22$$

$$T(Y) = T(30) = 1$$

$$K(A_1,S) = K(20,m) = .00207$$

then R = 5.22 x 1 x .00207 = .0108

and PC = R/(1 + R) = .011 or 1%.

Example 2   A typical male, exposed at age 55 to 19 rad of low-LET radiation to the esophagus, with a diagnosis of esophageal cancer at age 59, 4.6 years after exposure. Here D = 19, A_1 = 55, and Y = 4.

$$F = 19 + 19^2/116 = 22.11$$

$$T(4) = 0$$

$$K(55,m) = .000603$$

then $R = 0$

and $PC = 0$ also

Example 3 An esophageal cancer was diagnosed at age 44 in a woman follow-
ing several exposures to low-LET radiation at various ages. The first,
of one rad to the esophagus, occurred at age 20, 24 years and 2 months
before diagnosis ($Y = 24$). The second, to 2 rad, occurred 4 months later,
at the same age ($A_1 = 20$) but 23 years and 10 months before diagnosis,
($Y = 23$). At age 21, 23 years and 3 months before diagnosis, a 9-rad total
dose was received over a 36-hour period at the continuous rate of 250
millirad per hour ($Y = 23$). Finally, at age 35, three exposures, to 1.1,
0.6, and 0.7 rad, respectively, were received on consecutive days, 9
years and 2 months. prior to diagnosis ($Y = 9$).

The first, second, and third exposures should be considered separately,
because exposures 1 and 2 correspond to different values of Y, and exposures
2 and 3 to different exposure ages. The 9-rad continuous exposure delivered
over 36 hours should be treated as 2 exposures because it required more
than one day, but less than two. The suggested partition assigns a 3-rad
exposure to one 24-hour period and 6 rad to another. The three exposures
at age 35 can be treated as one because they correspond to the same values
of A_1 and Y, and because the total dose is less than 5 rad.

Exposure 1:

$$F(D) = 1 + 1^2/116 = 1.01$$

$$T(Y) = T(24) = 1$$

$$K(20,f) = .00562$$

$$R_1 = F \times T \times K = 1.01 \times 1 \times .00562 = .0057$$

Exposure 2:

$$F(2) = 2 + 2^2/116 = 2.03$$

$$T(23) = 1$$

$$K(20,f) = .00562$$

$$R_2 = F \times T \times K = 2.03 \times 1 \times .00562 = .0114$$

Exposure 3a:

$$F(3) = 3 + 3^2/116 = 3.08$$

$$T(23) = 1$$

$$K(21,f) = .00497$$

$$R_{3a} = F \times T \times K = 3.08 \times 1 \times .00497 = .0153$$

Exposure 3b:

$$F(6) = 6 + 6^2/116 = 6.31$$

$$T(23) = 1$$

$$K(21,f) = .00497$$

$$R_{3b} = F \times T \times K = 6.31 \times 1 \times .00497 = .0314$$

Exposures 4, 5, and 6:

$$F(1.1 + 0.6 + 0.7) = F(2.4) = 2.4 + 2.4^2/116 = 2.45$$

$$T(9) = .926$$

$$K(35,f) = .00153$$

$$R_{4,5,6} = F \times T \times K = 2.45 \times .926 \times .00153 = .0035$$

$$R = R_1 + R_2 + R_{3a} + R_{3b} + R_{4,5,6} = .0057$$

$$+ .0114 + .0153 + .0314 + .0035 = .0673$$

$$PC = R/(1+R) = .0673/1.0673 = .063 = 6\%.$$

The uncertainty surrounding PC estimates is discussed in Chapter VII, and Section VII-0 includes a derivation of approximate 90 percent credibility intervals for PC estimates.

To provide an orientation to the general magnitude of the PC values that result from the procedures described here, Fig X-4 has been drawn for tissue doses of 10 and 100 rad of low-LET radiation, and PC values plotted by age at exposure, for both males and females, and on the assumption that the minimal latent period has been satisfied. The vertical scale is logarithmic and curves are presented for only two radiation dose levels. For these and other reasons interpolation is to be discouraged.

Fig. X-4
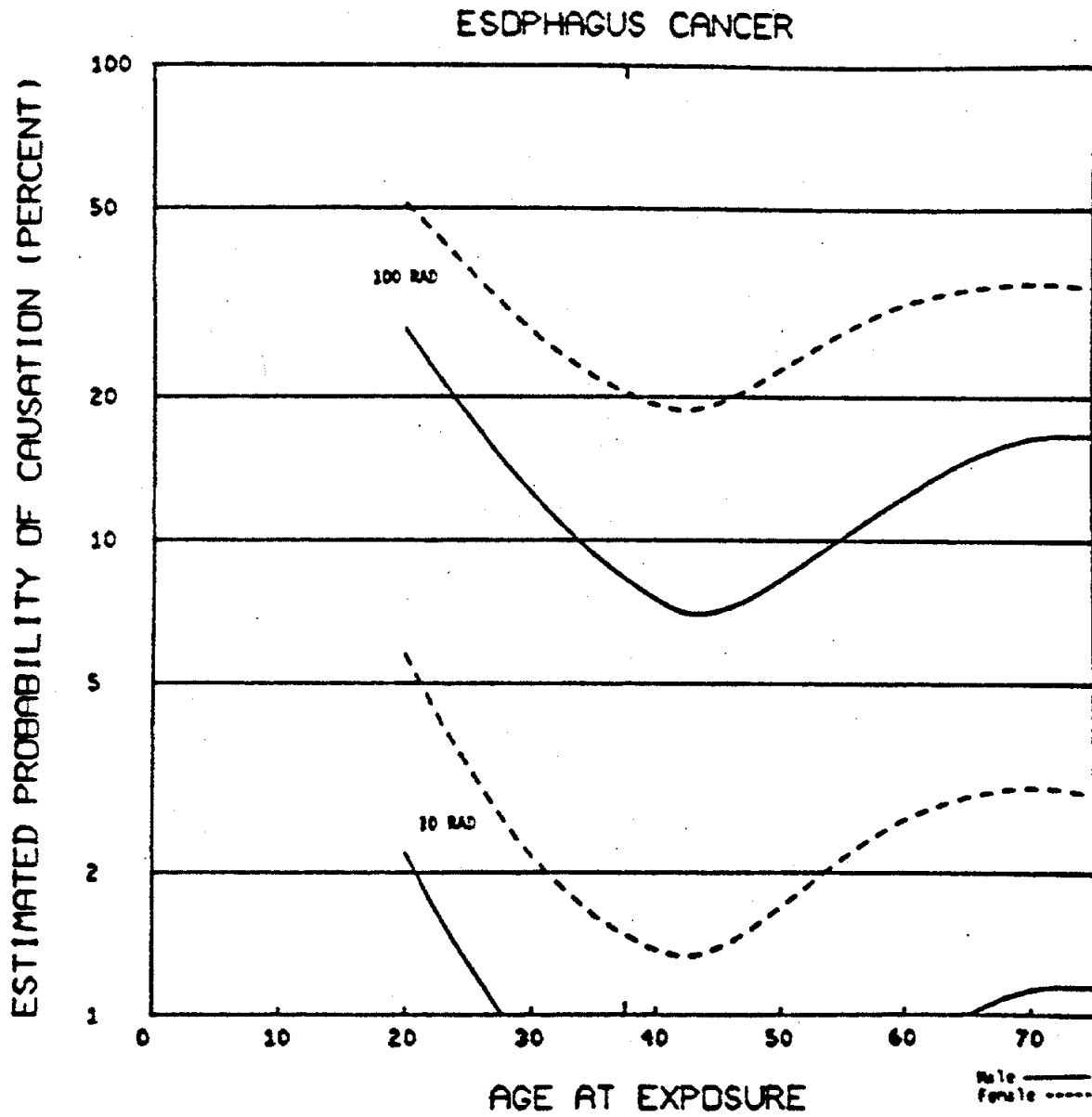
ESOPHAGUS CANCER

Table X-4.   Esophagus Cancer: Relative Excess $K(A_1, S)$
  by Exposure Age A_1 and Sex S

A_1	Sex		A_1	Sex	
	Male	Female		Male	Female
20	.00207	.00562	48	.000446	.00144
21	.00184	.00497	49	.000464	.00151
22	.00164	.00442	50	.000483	.00158
23	.00147	.00396	51	.000504	.00166
24	.00132	.00355	52	.000527	.00174
25	.00120	.00320	53	.000551	.00183
26	.00109	.00289	54	.000576	.00192
27	.000992	.00262	55	.000603	.00201
28	.000908	.00239	56	.000630	.00210
29	.000835	.00220	57	.000658	.00219
30	.000771	.00204	58	.000688	.00228
31	.000716	.00190	59	.000719	.00237
32	.000667	.00179	60	.000752	.00245
33	.000624	.00169	61	.000786	.00253
34	.000586	.00160	62	.000822	.00259
35	.000554	.00153	63	.000857	.00265
36	.000525	.00146	64	.000891	.00270
37	.000499	.00140	65	.000924	.00274
38	.000477	.00136	66	.000955	.00279
39	.000457	.00132	67	.000982	.00282
40	.000439	.00128	68	.00101	.00285
41	.000423	.00126	69	.00103	.00287
42	.000411	.00125	70	.00105	.00288
43	.000405	.00124	71	.00106	.00288
44	.000405	.00126	72	.00107	.00287
45	.000410	.00129	73	.00107	.00284
46	.000419	.00133	74	.00108	.00281
47	.000431	.00138	75	.00107	.00278

5. Stomach Cancer (151 in ICDA-8)

The risk coefficients used in the derivation of PC values for stomach cancer are taken from the BEIR III report (4) and adjusted to the period 11-30 years after exposure, but the BEIR coefficient for those exposed under age 10 is not used for reasons presented in Chapter VII. The inclusion of stomach cancer in the list of radiogenic cancers rests primarily on the experience of the British patients with ankylosing spondylitis treated by X rays (26) and of the A-bomb survivors (27) but is supported by animal experimentation (4). On the other hand, the recently published series on cervical cancer patients treated with X ray and radium had 201 observed cases of stomach cancer, several times the size of the ankylosing spondylitis series, but lacked evidence of a carcinogenic effect on stomach tissue (5). The relationship in the A-bomb survivors at the time the BEIR III report was prepared rested entirely on the experience of the Hiroshima survivors (27), but more recent data on the Nagasaki survivors indicate that the effect is by no means confined to the Hiroshima sample (28,29). The numbers are very large, 1754 deaths from stomach cancer through 1978, 1443 in Hiroshima, 311 in Nagasaki, but relative risk estimates are low: Kato and Schull estimate that only 42 of the deaths from stomach cancer may have been caused by radiation (28).

The Nagasaki Tumor Registry data on stomach cancer incidence were examined by Wakabayashi et al. for goodness of fit to the linear, linear-quadratic, and "pure" quadratic functions, and none of the models could be rejected by the usual statistical criterion (29). The Working Group has adopted the linear-quadratic dose-response function for stomach cancer as for most tumors in the expectation that further accumulation of data may in time demonstrate non-linearity, which is suggested by the combined A-bomb data of the two cities.

The Working Group has adopted the constant relative risk time-response model on the basis of Land and Tokunaga's analysis of other sites (33) and the demonstration by Kato and Schull (28) that, for all sites combined except leukemia, the picture is one of constant relative risk rather than absolute risk over time. (See also Chapter V-C.)

Environmental factors evidently play a dominant role in the etiology of stomach cancer, the incidence of which has been falling rapidly in the U.S. and many other countries, but few specific etiologic factors have been identified. The influence of smoking and alcohol is described as equivocal, but many studies have yielded crude associations between various aspects of diet and the risk of stomach cancer (34). There is no information on the joint effect of ionizing radiation and other risk factors. When the SEER incidence data, used here as the baseline data on the risk of stomach cancer, are examined by reporting area a wide range of variation is seen (Tables VII-1 and VII-2). As noted in Chapter IV-G and in Chapter IX, risk factors other than ionizing radiation may be taken into consideration in interpreting the PC values derived by the procedures presented here. If it is believed that some other risk factor operates additively with radiation, and the individual is thought to have been exposed to that risk factor to an extent greater than the average for the population generally, then the PC obtained from the present procedures may be somewhat excessive. But if it is believed that the second risk

factor may combine with radiation to enhance risk in multiplicative fashion, the PC estimates based on these procedures should be unbiassed. Caution should be exercised, however, because the appropriate interaction model for radiation in combination with any other carcinogens for stomach cancer is not known.

The calculational routine for stomach cancer is based on the assumptions and procedures detailed in Chapters V, VI, and IX. For stomach cancer the relative excess, R, in the basic equation

$$PC = R/(1 + R)$$

is found as the product of three functions, i.e.,

$$R = F(D) \times T(Y) \times K(A_1,S)$$

where $F(D)$ represents the contribution of a low-LET radiation dose to the relevant tissue (D), $T(Y)$ represents the conditioning influence of years from exposure to diagnosis, and $K(A_1,S)$ represents the standardized relative excess risk of stomach cancer per rad for a person of sex S and age at exposure A_1, when both F and $T = 1$.

Under the linear-quadratic model assumed for stomach cancer when exposure is to low-LET radiation,

$$F = D + D^2/116.$$

For the stomach the influence of time (T) on the relative risk depends only on years from exposure to diagnosis (Y). The function T is tabled below.

Y	0-4	5	6	7	8	9	10+
T	0	.074	.259	.500	.741	.926	1

The standardized relative risk of excess cancer, K, is given in the accompanying Table X-5 for low-LET radiation and for each sex and year of age (completed years) from 10 to 75.

A few examples should make it clear how PC values are to be obtained for stomach cancer.

Example 1   A typical woman aged 25 with an exposure of 10 rad of X rays to the stomach, and with a diagnosis of stomach cancer at age 50, 25 years later. Then $D = 10$, $A_1 = 25$, and $Y = 25$.

$$F(10) = 10 + 10^2/116 = 10.86$$

$$T(25) = 1$$

$$K(25,f) = .00782$$

then $R = F \times T \times K = 10.86 \times 1 \times .00782 = .0849$

and $PC = R/(1 + R) = .0849/1.0849 = .078$ or 8%.

Example 2   A stomach cancer was diagnosed at age 44 in a woman following several exposures to low-LET radiation at various ages. The first, of one rad to the stomach, occurred at age 20, 24 years and 2 months before diagnosis (Y = 24). The second, to 2 rad, occurred 4 months later, at the same age (A_1=20) but 23 years and 10 months before diagnosis (Y = 23). At age 21, 23 years and 3 months before diagnosis, a 9-rad total dose was received over a 36-hour period at the continuous rate of 250 millirad per hour (Y = 23). Finally, at age 35, three exposures, to 1.1, 0.6, and 0.7 rad, respectively, were received on consecutive days, 9 years and 2 months prior to diagnosis (Y = 9).

The first, second, and third exposures should be considered separately, because exposures 1 and 2 correspond to different values of Y, and exposures 2 and 3 to different exposure ages. The 9-rad continuous exposure delivered over 36 hours should be treated as 2 exposures because it required more than one day, but less than two. The suggested partition assigns a 3-rad exposure to one 24-hour period and 6 rad to another. The three exposures at age 35 can be treated as one because they correspond to the same values of A_1 and Y, and because the total dose is less than 5 rad.

Exposure 1:

$$F(1) = 1 + 1^2/116 = 1.01$$

$$T(24) = 1$$

$$K(20,f) = .0100$$

$$R_1 = F \times T \times K = 1.01 \times 1 \times .0100 = .0101$$

Exposure 2:

$$F(2) = 2 + 2^2/116 = 2.03$$

$$T(23) = 1$$

$$K(20,f) = .0100$$

$$R_2 = F \times T \times K = 2.03 \times 1 \times .0100 = .0203$$

Exposure 3a:

$$F(3) = 3 + 3^2/116 = 3.08$$

$$T(23) = 1$$

$$K(21,f) = .00959$$

$$R_{3a} = F \times T \times K = 3.08 \times 1 \times .00959 = .0295$$

Exposure 3b:

$$F(6) = 6 + 6^2/116 = 6.31$$

$$T(23) = 1$$

$$K(21,f) = .00959$$

$$R_{3b} = F \times T \times K = 6.31 \times 1 \times .00959 = .0605$$

Exposures 4, 5, and 6:

$$F(1.1 + 0.6 + 0.7) = F(2.4) = 2.4 + 2.4^2/116 = 2.45$$

$$T(9) = .926$$

$$K(35,f) = .00458$$

$$R_{4,5,6} = F \times T \times K = 2.45 \times .926 \times .00458 = .0104$$

$$R = R_1 + R_2 + R_{3a} + R_{3b} + R_{4,5,6} = .0101$$

$$+ .0203 + .0295 + .0605 + .0104 = .131$$

$$PC = R/(1 + R) = .131/1.131 = .116 = 12\%$$

The uncertainty surrounding PC estimates is discussed in Chapter VII, and Section VII-0 includes a derivation of approximate 90 percent credibility intervals for PC estimates.

To provide an orientation to the general magnitude of the PC values that result from the procedures described here, Fig X-5 has been drawn for tissue doses of 1, 10, and 100 rad of low-LET radiation, and PC values plotted by age at exposure, for both males and females, and on the assumption that the minimal latent period has been satisfied. The vertical scale is logarithmic and curves are presented for only three radiation dose levels. For these and other reasons interpolation is to be discouraged.

Fig. X-5

STOMACH CANCER

(Y-axis: ESTIMATED PROBABILITY OF CAUSATION (PERCENT); X-axis: AGE AT EXPOSURE; curves labeled 100 RAD, 10 RAD, 1 RAD; legend: Male ——, Female ----)
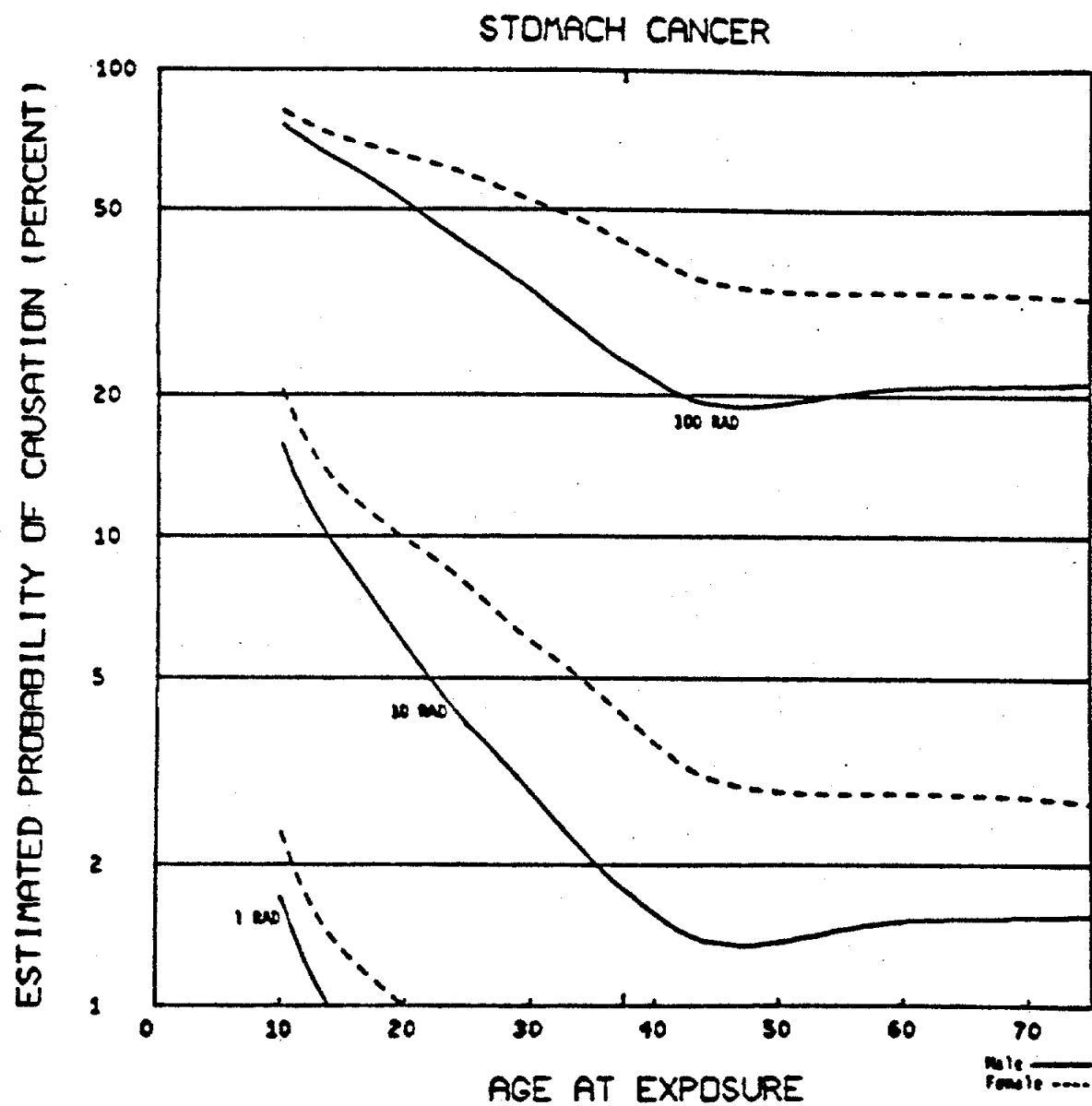
Table X-5. Stomach Cancer: Relative Excess $K(A_1, S)$ by Exposure Age A_1 and Sex S

A_1	Sex		A_1	Sex	
	Male	Female		Male	Female
10	.0172	.0238	43	.00131	.00302
11	.0145	.0201	44	.00129	.00294
12	.0125	.0175	45	.00127	.00287
13	.0111	.0156	46	.00126	.00282
14	.00995	.0142	47	.00126	.00278
15	.00907	.0132	48	.00126	.00276
16	.00826	.0124	49	.00127	.00274
17	.00751	.0117	50	.00128	.00272
18	.00684	.0111	51	.00129	.00271
19	.00623	.0105	52	.00130	.00270
20	.00569	.0100	53	.00132	.00270
21	.00522	.00959	54	.00134	.00270
22	.00479	.00915	55	.00135	.00270
23	.00442	.00872	56	.00137	.00270
24	.00410	.00827	57	.00138	.00270
25	.00381	.00782	58	.00140	.00270
26	.00356	.00736	59	.00141	.00270
27	.00333	.00692	60	.00142	.00270
28	.00311	.00652	61	.00142	.00270
29	.00290	.00616	62	.00143	.00270
30	.00270	.00585	63	.00143	.00269
31	.00251	.00558	64	.00143	.00269
32	.00234	.00533	65	.00143	.00268
33	.00218	.00508	66	.00143	.00267
34	.00204	.00483	67	.00143	.00267
35	.00192	.00458	68	.00144	.00266
36	.00180	.00434	69	.00144	.00266
37	.00171	.00410	70	.00144	.00265
38	.00162	.00388	71	.00144	.00263
39	.00154	.00367	72	.00144	.00262
40	.00147	.00348	73	.00145	.00260
41	.00141	.00330	74	.00145	.00258
42	.00135	.00314	75	.00145	.00257

6. Colon Cancer (153 in ICDA-8)

The colon has long been considered an organ of apparent, but uncertain, sensitivity to radiation carcinogenesis, based on studies of patient populations irradiated for benign or malignant pelvic disease and the British series of patients treated with radiation for ankylosing spondylitis. The uncertainty arose because, although remarkable excess risks were seen in some studies (35,36), there was none in others with comparable levels of exposure (37,38). Moreover, the excess risk seen among spondylitis patients treated with X rays was discounted because of known associations among spondylitis, ulcerative colitis, and colon cancer (3,26). In fact, an excess risk was seen soon after treatment began, well before the expiration of a 10-, or even 5-year, minimum induction period for radiation-induced cancer.

More recently, excess colon cancer has been observed in mortality data for survivors of the Hiroshima A-bomb (28) and in tumor-registry data for survivors of the Nagasaki bomb (29). At about the same time, however, in a large international series of women in Europe and North America treated by irradiation for cervical cancer, no excess mortality was seen for colon cancer despite an average dose of about 500 rad to the colon, possibly because average follow-up is only 7.6 years (5).

At the present time the evidence for excess colon cancer associated with radiation exposure rests mainly upon the A-bomb survivor data, perhaps because colon cancer normally is rare in Japan in comparison with the United States, and a modest excess may therefore be easier to detect. The most recent A-bomb survivor data are consistent with the risk estimates given in the 1980 BEIR report (4,23) except that the data do not appear adequate to support a risk estimate for exposures before age 20 (see Chapter VII-F). The BEIR III coefficients for ages 20+, adjusted to the period 11-30 years after exposure, are the basic risk estimates used by the Working Group.

There has been no analysis of colon cancer to establish the most appropriate dose-response function or to determine whether the relative risk model is superior to the absolute risk model for distributing radiogenic cases over time. The Working Group has assumed that the preferred linear-quadratic dose-response model of the BEIR III committee and the constant relative risk time-response model would provide a suitable basis for the calculation of PC values for this site. These general assumptions are discussed in Chapter V.

The normal incidence of colon cancer in the U.S. is best represented by the SEER data of the National Cancer Institute which, however, are subject to some variation among reporting areas (8). (See Chapter VII-C and Tables VII-1 and VII-2.) The base-line rates employed here are those for all races combined and for all areas combined except for Puerto Rico, and are age- and sex-specific. They are taken from computer tapes for the period 1973-1981.

Migrant studies have underscored the role environmental factors, including nutrition, must play in the etiology of colon cancer, especially the dietary intake of meat and animal fat. Epidemiologic studies have

also identified a number of familial and hereditary factors that influence the risk of colon cancer and have shown that persons with chronic ulcerative colitis are at high risk of colon cancer (39). For none of these factors are quantitative estimates of relative risk firm enough for specific guidance in this context. Nor is there information on any interaction between such risk factors and radiation in the etiology of colon cancer. As noted in Chapter IV-G and in Chapter IX, risk factors other than ionizing radiation may be taken into consideration in interpreting the PC values derived by the procedures presented here. If it is believed that some other risk factor operates additively with radiation, and if the individual is thought to have been exposed to that risk factor to an extent greater than the average for the population generally, then the PC obtained from the present procedures may be somewhat excessive. But if it is believed that the second risk factor may combine with radiation to enhance risk in multiplicative fashion, the PC estimates based on these procedures should be unbiassed.

The procedures for calculating PC values for colon cancer rest on the general strategy outlined in Chapters V, VI, and IX. For colon cancer, as for other sites, the relative excess, R, in the basic equation

$$PC = R/(1 + R)$$

is found as the product of three functions, i.e.,

$$R = F(D) \times T(Y) \times K(A_1,S)$$

where $F(D)$ represents the influence of the low-LET tissue dose (D), $T(Y)$ represents the influence of years from exposure to the diagnosis of colon cancer (Y), and $K(A_1,S)$ represents the relative excess risk of colon cancer for a person of age at exposure A_1 and sex S, when both F and T = 1.

Under the linear-quadratic model assumed for colon cancer when exposure is to low-LET radiation

$$F = D + D^2/116.$$

For colon cancer the influence of time (T) on the relative risk depends entirely on years from exposure to diagnosis (Y). The function T is tabulated below:

Y	0-4	5	6	7	8	9	10+
T	0	.074	.259	.500	.741	.926	1

The standardized relative risk of excess colon cancer, K, is given in the accompanying Table X-6 for low-LET radiation, for each sex and completed year of age from 20 to 75.

A few specific examples should illustrate the way in which PC values for colon cancer may be derived from the material presented here.

Example 1   A typical female aged 45 given 5 rad of low-LET radiation to the colon, with a diagnosis of colon cancer at age 48, 3.5 years after

exposure. Then D = 5, A_1 = 45, and Y = 3.

$$F(5) = 5 + 5^2/116 = 5.22$$

$$T(3) = 0$$

$$K(45,f) = .000340$$

$$\text{then } R = F \times T \times K = 0$$

$$\text{and } PC = 0 \text{ also.}$$

Example 2   A typical male exposed to an acute dose of 2 rad of low-LET radiation to the colon at age 36, and with a diagnosis of colon cancer at age 55. Then D = 2, A_1 = 36, and Y = 19.

$$F(2) = 2 + 2^2/116 = 2.03$$

$$T(19) = 1$$

$$K(36,m) = .000493$$

$$\text{then } R = F \times T \times K = 2.03 \times 1 \times .000493 = .0010$$

$$\text{and } PC = R/(1 + R) = .0010/1.0010 = .001 = 0.1\%$$

Example 3   A colon cancer was diagnosed at age 44 in a woman following several exposures to low-LET radiation at various ages. The first, of one rad to the colon, occurred at age 20, 24 years and 2 months before diagnosis (Y = 24). The second, to 2 rad, occurred 4 months later, at the same age (A_1 = 20) but 23 years and 10 months before diagnosis (Y = 23). At age 21, 23 years and 3 months before diagnosis, a 9-rad total dose was received over a 36-hour period at the continuous rate of 250 millirad per hour (Y=23). Finally, at age 35, three exposures, to 1.1, 0.6, and 0.7 rad, respectively, were received on consecutive days, 9 years and 2 months prior to diagnosis (Y = 9).

The first, second, and third exposures should be considered separately, because exposures 1 and 2 correspond to different values of Y, and exposures 2 and 3 to different exposure ages. The 9-rad continuous exposure delivered over 36 hours should be treated as 2 exposures because it required more than one day, but less than two. The partition giving the maximum risk estimate assigns a 3-rad exposure to one 24-hour period and 6 rad to another. The three exposures at age 35 can be treated as one because they correspond to the same values of A_1 and Y, and because the total dose is less than 5 rad.

Exposure 1:

$$F(1) = 1 + 1^2/116 = 1.01$$

$$T(24) = 1$$

$$K(20,f) = .00153$$

$$R_1 = F \times T \times K = 1.01 \times 1 \times .00153 = .00155$$

- 213 -

Exposure 2:

$$F(2) = 2 + 2^2/116 = 2.03$$

$$T(23) = 1$$

$$K(20,f) = .00153$$

$$R_2 = F \times T \times K = 2.03 \times 1 \times .00153 = .00311$$

Exposure 3a:

$$F(3) = 3 + 3^2/116 = 3.08$$

$$T(23) = 1$$

$$K(21,f) = .00143$$

$$R_{3a} = F \times T \times K = 3.08 \times 1 \times .00143 = .00440$$

Exposure 3b:

$$F(6) = 6 + 6^2/116 = 6.31$$

$$T(23) = 1$$

$$K(21,f) = .00143$$

$$R_{3b} = F \times T \times K = 6.31 \times 1 \times .00143 = .00902$$

Exposures 4, 5, and 6:

$$F(1.1 + 0.6 + 0.7) = F(2.4) = 2.4 + 2.4^2/116 = 2.45$$

$$T(9) = .926$$

$$K(35,f) = .000558$$

$$R_{4,5,6} = F \times T \times K = 2.45 \times .926 \times .000558 = .00127$$

$$R = R_1 + R_2 + R_{3a} + R_{3b} + R_{4,5,6} = .00155$$

$$+ .00311 + .00440 + .00902 + .00127 = .0194$$

$$PC = R/(1+R) = .0194/1.0194 = .0190 \text{ or } 2\%.$$

The uncertainty surrounding PC estimates is discussed in Chapter VII, and Section VII-0 includes a derivation of approximate 90 percent credibility intervals for PC estimates.

To provide an orientation to the general magnitude of the PC values that result from the procedures described here, Fig. X-6 has been drawn for tissue doses of 10 and 100 rad of low-LET radiation, and PC values

plotted by age at exposure, for both males and females, and on the assumption that the minimal latent period has been satisfied. The vertical scale is logarithmic and curves are presented for only two radiation dose levels. For these and other reasons interpolation is to be discouraged.

Fig. X-6
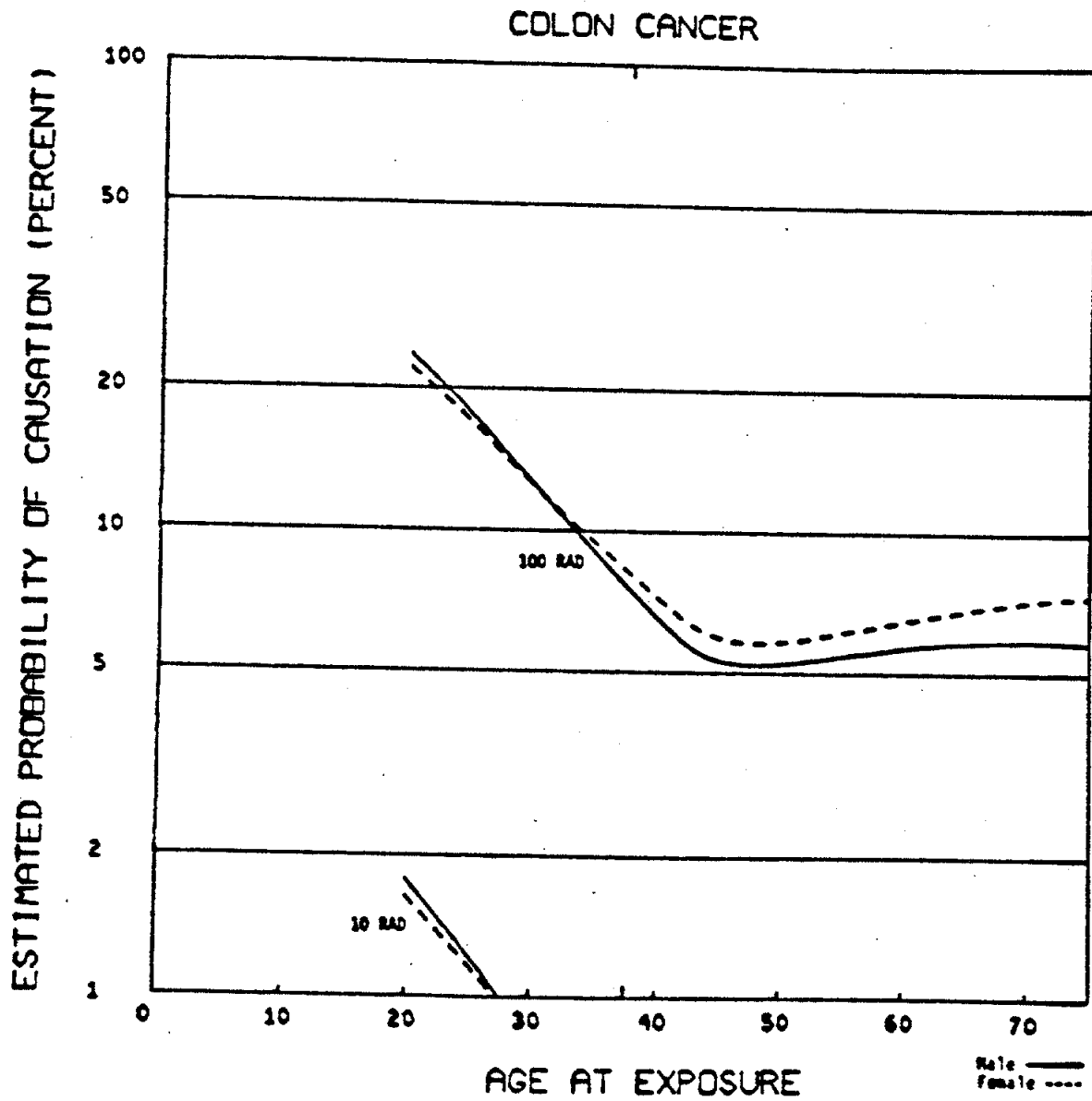
COLON CANCER

Table X-6. Colon Cancer: Relative Excess $K(A_1,S)$
by Exposure Age A_1 and Sex S

A_1	Sex		A_1	Sex	
	Male	Female		Male	Female
20	.00167	.00153	48	.000296	.000331
21	.00155	.00143	49	.000296	.000331
22	.00144	.00134	50	.000298	.000333
23	.00134	.00125	51	.000300	.000335
24	.00124	.00117	52	.000302	.000338
25	.00115	.00109	53	.000305	.000342
26	.00106	.00102	54	.000307	.000346
.27	.000979	.000947	55	.000310	.000350
28	.000905	.000882	56	.000313	.000354
29	.000837	.000822	57	.000316	.000359
30	.000774	.000768	58	.000319	.000363
31	.000716	.000718	59	.000321	.000368
32	.000663	.000673	60	.000324	.000372
33	.000615	.000631	61	.000326	.000377
34	.000571	.000593	62	.000328	.000381
35	.000530	.000558	63	.000330	.000385
36	.000493	.000526	64	.000332	.000389
37	.000460	.000496	65	.000333	.000393
38	.000429	.000468	66	.000334	.000397
39	.000401	.000442	67	.000335	.000402
40	.000376	.000418	68	.000336	.000406
41	.000353	.000395	69	.000336	.000410
42	.000333	.000375	70	.000336	.000414
43	.000319	.000359	71	.000336	.000417
44	.000309	.000348	72	.000335	.000419
45	.000302	.000340	73	.000334	.000421
46	.000298	.000335	74	.000333	.000423
47	.000296	.000332	75	.000332	.000423

7. Cancer of the Liver (155.0 and 197.8 in ICDA-8)

Primary cancer of the liver is well known as a late effect of radiography employing the contrast medium, Thorotrast, a colloidal thorium dioxide compound emitting alpha particles (2,4,40). There is, however, some uncertainty as to the etiologic significance of its chemical vs. its radiation properties. Human data on the association between ionizing radiation and liver cancer are otherwise sparse. In the British series of ankylosing spondylitis patients treated by X rays no excess liver cancer was found, but the liver was classified as one of the "lightly irradiated sites", for which the observed numbers of deaths from cancer were not significantly greater than expectation based on the British mortality statistics (3). The 1977 UNSCEAR report (2) provides a "tentative risk assessment" of 10-20 excess cancers per million persons per rad of alpha radiation. With a mean latency of 25 years these coefficients become approximately 0.40 to 0.80 per million per year per rad. The BEIR III report (4) provides an estimate of 300 per million persons per rad of alpha radiation, 15 per million persons per rad of low-LET radiation on the assumption of a RBE of 20, and an annualized risk coefficient of 0.70 excess cancers per million per year per rad of low-LET radiation.

The most extensive human data on liver cancer following external exposure to ionizing radiation derive from the experience of the Japanese A-bomb survivors: 55 incident cases in Nagasaki (29) and 118 in Hiroshima (30). The Nagasaki Tumor Registry report for 1959-1978 yields a risk estimate of 0.70 ± 0.52 excess cancers per million persons per year per rad (29), and the Hiroshima Tumor Registry for the same period an estimate of 0.72 ± .18 (30). The death certificate diagnoses for the Life Span Study sample of 82,000 A-bomb survivors have not been tabulated for liver cancer in the most recent report (1950-1978) (28) but cancers of the liver are included in the category of "other or unspecified digestive organs," that is, cancers of digestive organs other than the esophagus, stomach, pancreas, colon, and rectum and rectosigmoid junction. Thus, cancer of the liver is a significant part of the "all other" category that includes 595 deaths and for which a test of trend with dose returns a highly significant p of .0033.

None of the reports cited provides age- or sex-specific risk estimates for cancer of the liver, but trend tests on the age-specific mortality tables of Kato and Schull (28) for "all other" gastrointestinal organs yield p-values as follows for the observed numbers of deaths in tests of the relation between mortality and dose:

Age at exposure	Number of deaths	p in Test of Trend with Dose
0-9	4	.64
10-19	30	.02
20-34	82	.08
35-49	284	.04
50+	195	.20

The sex-specific tests of trend with dose result in p-values of .03 for males and .02 for females (28).

Overall, the more recent data support the BEIR III risk coefficients for liver cancer, except that the data are too fragile, for persons exposed under age 20, for the BEIR estimate for that age-group to be used (see Chapter VII-F). The BEIR III coefficients have been adjusted to the period 11-30 years after exposure.

Neither dose-response nor time-response has been adequately investigated for cancer of the liver and, except for the Thorotrast patients, whose irradiation is essentially continuous, there are too few cases of radiogenic liver cancer for such analyses. Accordingly, the Working Group has assumed that the appropriate dose-response functions are linear-quadratic for low-LET and linear for high-LET radiation and the appropriate time-response function the constant relative risk model.

The baseline risk of liver cancer in the US population has been taken from the data of the SEER program of the National Cancer Institute for the years 1973-1981. Published data from the contributing registries for the years 1973-1977 (8) reveal great variation (see Tables VII-1 and VII-2) and it should be stressed that it is the set of rates for all areas (except Puerto Rico) combined and for all races combined that is used in the calculations here.

Although ionizing radiation is clearly a risk factor for liver cancer, there are far more important risk factors. These include exposure to arsenic, vinyl chloride, probably hepatitis B virus, and alcohol (41). For none of these factors are quantitative estimates of relative risk firm enough for specific guidance in this context. Nor is there information on any interaction between such risk factors and radiation in the etiology of liver cancer. As noted in Chapter IV-G and in Chapter IX, risk factors other than ionizing radiation may be taken into consideration in interpreting the PC values derived by the procedures presented here. If it is believed that some other risk factor operates additively with radiation, and the individual is thought to have been exposed to that risk factor to an extent greater than the average for the population generally, then the PC obtained from the present procedures may be somewhat excessive. But if it is believed that the second risk factor may combine with radiation to enhance risk in multiplicative fashion, the PC estimates based on these procedures should be unbiassed.

The procedures for calculating PC values for liver cancer are based on the assumptions and principles of Chapter V and the procedures of Chapters VI and IX. As with most other sites, for liver cancer the relative excess, R, in the basic equation

$$PC = R/(1 + R)$$

is found as the product of three functions, i.e.,

$$R = F(D) \times T(Y) \times K(A_1,S)$$

where F(D) represents the influence of the tissue dose (D) in rad of low-

- 219 -

LET radiation, T(Y) represents the variation in R over time in years (Y) after exposure, and K(A$_1$,S) represents the relative excess risk of liver cancer for a person of age at exposure A$_1$ and sex S, when both F and T = 1.

Under the linear-quadratic model assumed for liver cancer, when exposure is to low-LET radiation

$$F = D + D^2/116.$$

For liver cancer the influence of time (T) on the relative risk depends entirely on years from exposure to diagnosis (Y). The function T is tabled below:

Y	0-4	5	6	7	8	9	10+
T	0	.074	.259	.500	.741	.926	1.

The standardized relative risk of excess liver cancer, K, is given in the accompanying Table X-7 for low-LET radiation and for each sex and year of completed age from 20 to 75. A few examples should clarify the actual computational procedures for liver cancer following exposure to ionizing radiation.

Example 1   A typical male, exposed at age 31 to 10 rad of low-LET radiation to the liver, with diagnosis of liver cancer at age 59. Then D = 10, A$_1$ = 31, and Y = 28.

$$F(D) = 10 + 10^2/116 = 10.86$$

$$T(Y) = T(28) = 1$$

$$K(A_1,S) = K(31,m) = .00755$$

then R = F x T x K = 10.86 x 1 x .00755 = .0820

and PC = R/(1 + R) = .0820/1.0820 = .076 or 8%.

Example 2   A typical female given 10 rad of low-LET radiation to the liver at age 36, with a diagnosis of liver cancer at age 55, 19 years after exposure. Then D = 10, A$_1$ = 36, and Y = 19.

$$F(10) = 10 + 10^2/116 = 10.86$$

$$T(19) = 1$$

$$K(36,f) = .0129$$

then R = F x T x K = 10.86 x 1 x .0129 = .140

and PC = R/(1+R) = .140/(1.140) = .123 or 12%.

Example 3   A liver cancer was diagnosed at age 44 in a woman following several exposures to low-LET radiation at various ages. The first, of one rad to the liver, occurred at age 20, 24 years and 2 months before

diagnosis (Y = 24). The second, to 2 rad, occurred 4 months later, at the same age (A_1 = 20) but 23 years and 10 months before diagnosis (Y = 23). At age 21, 23 years and 3 months before diagnosis, 9 rad total dose was received over a 36-hour period at the continuous rate of 250 millirad per hour (Y = 23). Finally, at age 35, three exposures, to 1.1, 0.6, and 0.7 rad, respectively, were received on consecutive days, 9 years and 2 months prior to diagnosis (Y = 9).

The first, second, and third exposures should be considered separately, because exposures 1 and 2 correspond to different values of Y, and exposures 2 and 3 to different exposure ages. The 9-rad continuous exposure delivered over 36 hours should be treated as 2 exposures because it required more than one day, but less than two. The suggested partition assigns a 3-rad exposure to one 24-hour period and 6 rad to another. The three exposures at age 35 can be treated as one because they correspond to the same values of A_1 and Y, and because the total dose is less than 5 rad.

Exposure 1:

$$F(D) = F(1) = 1 + 1^2/116 = 1.01$$

$$T(Y) = T(24) = 1$$

$$K(20,f) = .0503$$

$$R_1 = F \times T \times K = 1.01 \times 1 \times .0503 = .0508$$

Exposure 2:

$$F(2) = 2 + 2^2/116 = 2.03$$

$$T(23) = 1$$

$$K(20,f) = .0503$$

$$R_2 = F \times T \times K = 2.03 \times 1 \times .0503 = .102$$

Exposure 3a:

$$F(3) = 3 + 3^2/116 = 3.08$$

$$T(23) = 1$$

$$K(21,f) = .0463$$

$$R_{3a} = F \times T \times K = 3.08 \times 1 \times .0463 = .143$$

Exposure 3b:

$$F(6) = 6 + 6^2/116 = 6.31$$

$$T(23) = 1$$

$$K(21,f) = .0463$$

$$R_{3b} = F \times T \times K = 6.31 \times 1 \times .0463 = .292$$

Exposures 4, 5, and 6:

$$F(1.1 + 0.6 + 0.7) = F(2.4) = 2.4 + 2.4^2/116 = 2.45$$

$$T(9) = .926$$

$$K(35,f) = .0139$$

$$R_{4,5,6} = F \times T \times K = 2.45 \times .926 \times .0139 = .0315$$

$$R = R_1 + R_2 + R_{3a} + R_{3b} + R_{4,5,6} = .0508 + .102$$

$$+ .143 + .292 + .0315 = .619$$

$$PC = R/(1+R) = .619/1.619 = .382 = 38\%$$

The uncertainty surrounding PC estimates is discussed in Chapter VII, and Section VII-0 includes a derivation of approximate 90 percent credibility intervals for PC estimates.

To provide an orientation to the general magnitude of the PC values that result from the procedures described here, Fig X-7 has been drawn for tissue doses of 1, 10, and 100 rad of low-LET radiation, and PC values plotted by age at exposure, for both males and females, and on the assumption that the minimal latent period has been satisfied. The vertical scale is logarithmic and curves are presented for only three radiation dose levels. For these and other reasons interpolation is to be discouraged.

Fig. X-7
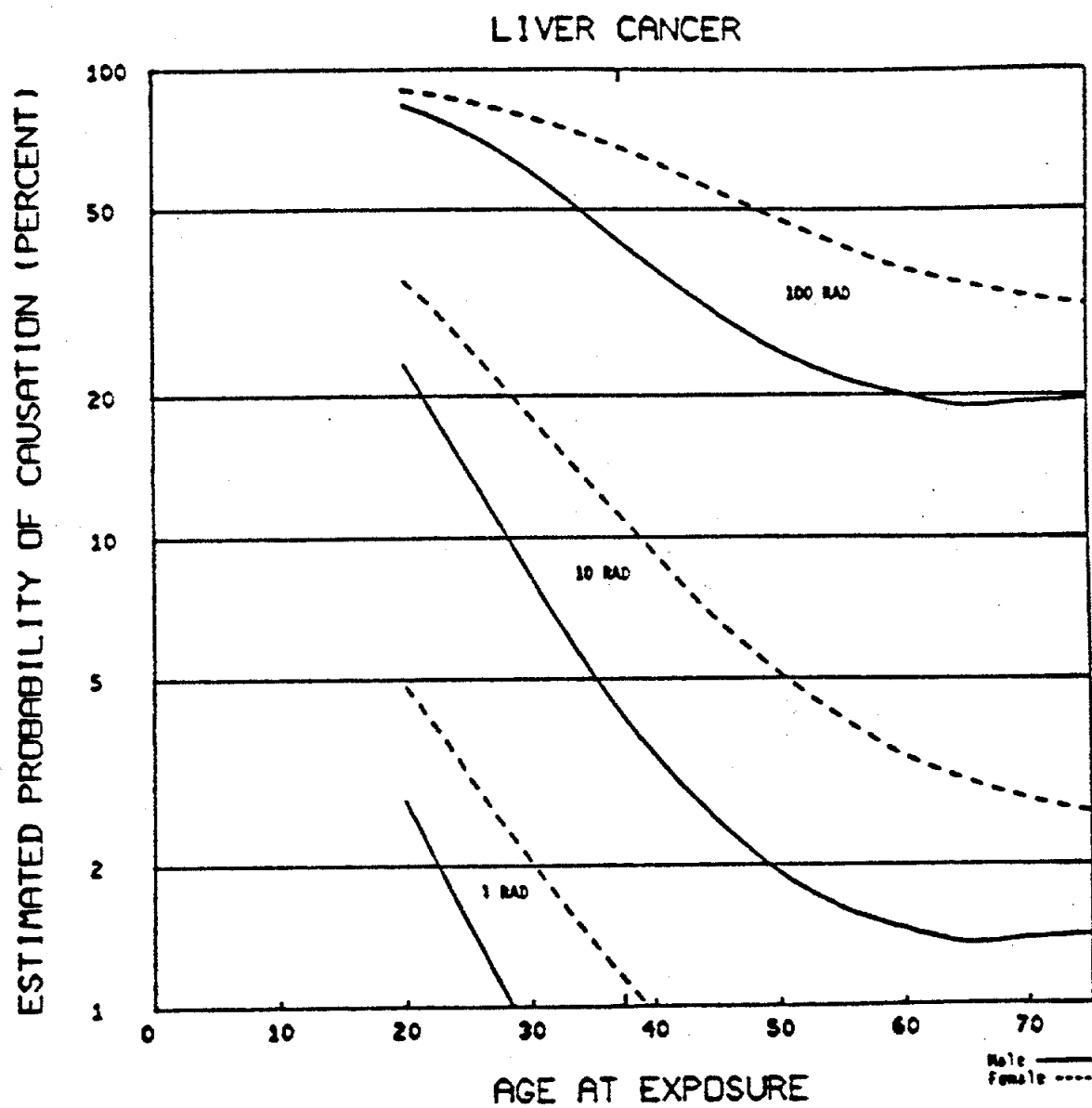
LIVER CANCER

Table X-7. Liver Cancer: Relative Excess $K(A_1,S)$ by Exposure Age A_1 and Sex S

A_1	Sex		A_1	Sex	
	Male	Female		Male	Female
20	.0281	.0503	48	.00199	.00559
21	.0246	.0463	49	.00190	.00530
22	.0216	.0424	50	.00181	.00503
23	.0191	.0387	51	.00174	.00478
24	.0170	.0352	52	.00167	.00455
25	.0151	.0320	53	.00161	.00435
26	.0134	.0292	54	.00156	.00415
27	.0119	.0267	55	.00152	.00397
28	.0106	.0244	56	.00148	.00380
29	.00943	.0224	57	.00144	.00365
30	.00843	.0206	58	.00141	.00350
31	.00755	.0189	59	.00138	.00337
32	.00678	.0175	60	.00136	.00326
33	.00612	.0162	61	.00133	.00317
34	.00555	.0150	62	.00131	.00309
35	.00504	.0139	63	.00129	.00301
36	.00460	.0129	64	.00127	.00295
37	.00421	.0119	65	.00126	.00288
38	.00387	.0111	66	.00126	.00283
39	.00357	.0103	67	.00126	.00277
40	.00331	.00954	68	.00127	.00272
41	.00308	.00884	69	.00128	.00267
42	.00287	.00819	70	.00128	.00263
43	.00269	.00762	71	.00129.	.00258
44	.00252	.00712	72	.00130	.00255
45	.00237	.00667	73	.00130	.00251
46	.00223	.00627	74	.00131	.00248
47	.00210	.00591	75	.00131	.00246

8. Cancer of the Pancreas (157 in ICDA-8)

Risk estimates for pancreatic cancer are less reliable than those for most sites, perhaps because most data are derived from death certificate diagnoses that do not fare well in pathology reviews. The UNSCEAR (2) and BEIR III (4) reports rely heavily on the excess reported for the British ankylosing spondylitis patients treated with X rays (26), but the relationship is weak in the most recent report on that series (3). The pancreas was a "heavily irradiated site," and although Doll and his colleagues have yet to publish a dose estimate for the pancreas, the BEIR III report gives a value of 90 rad. There were 18 deaths from pancreatic cancer vs. 9.5 expected in the latest report, but 5 occurred within the first two years after treatment (vs. 1 expected) and the 13 vs. 8.5 comparison for the period 3+ years after therapy returns a p-value in excess of .10. Land has calculated an estimate of $0.70 \pm .61$ excess deaths per million per year per rad for this experience (23). The BEIR III estimate is .90 for males and .99 for females, with age-specific coefficients varying in direct proportion to those for all gastrointestinal cancer deaths among the A-bomb survivors, 1950-1974.

Death certificate diagnoses for the large Life Span Study sample of A-bomb survivors reveal no statistical evidence that the risk of pancreatic cancer depends on dose (p = .67 in a test of linear trend on 148 deaths) (28), but the pathology confirmation and detection percentages for cancer of the pancreas are low, 62 and 37 respectively, in a series of 61 autopsy cases (42). In a report on 36 cases in the Nagasaki Tumor Registry series for 1959-1978, Wakabayashi et al. report a trend p of .06, for which the risk coefficient is $1.15 \pm .92$ (29). In the unpublished Hiroshima Tumor Registry report for the same time period there are 143 cases with a non-significant risk coefficient of .18 (90-percent confidence interval of -.14 to +.50) (30). Overall, therefore, the experience of the A-bomb survivors provides very weak support for a relationship between pancreatic cancer and radiation dose.

In their first report on deaths among workers at the Hanford Works in Richland, Washington, Mancuso et al. reported a probable excess of 6 deaths from pancreatic cancer among 31, and estimated the doubling dose at 7.4 rad (43). The statistical significance of the association was verified by Hutchison et al. in independent calculations (44) and by Gilbert and Marks in a cohort analysis of the worker population (45). These and numerous other commentators stressed the fragility of the data (death certificate diagnosis and the likelihood of exposure to carcinogenic chemicals). The association was later weakened by the finding that, for 1 of the 4 critical deaths in the 15+ rem dose group, medical records showed that the primary cancer was probably in the stomach (46).

The pancreas barely meets the criteria for inclusion among the sites for which PC estimates are to be made. There are human data from which the necessary risk coefficients can be derived, but the statistical reliability of the association between cancer and dose is low and consistency among the few available series is minimal.

The Working Group chose to employ the BEIR III coefficients except for exposure before the age of 20, the basis for the BEIR III coefficient

for younger individuals having been judged insufficient for the present purpose (Chapter VII-F). The BEIR coefficients were, however, adjusted to the period 11-30 years after exposure. There appears to be no published analysis of dose-response functions appropriate for the pancreas, and the available data are too few to make such analysis very meaningful. Accordingly, the Working Group has employed the preferred linear-quadratic dose-response model for this site as for most of the solid tumors. Similarly, although time-response models have not been explored, the Working Group considered that the constant relative risk model was a reasonable choice.

The baseline data needed for the calculation of PC values have been taken from the data tapes for the SEER program of the National Cancer Institute for the years 1973-1981 and for all races combined and all areas combined except Puerto Rico. Published data for the reporting areas in the period 1973-1977 show only a moderate degree of variation, but an appreciable difference between the sexes, males having the higher rates (8). (See Tables VII-1 and VII-2.)

Cancer of the pancreas is also associated with alcohol consumption, exposure to certain chemicals, and smoking (47). The Working Group found no information on the pattern of interaction between such well-established risk factors and radiation. As noted in Chapter IV-G and in Chapter IX, risk factors other than ionizing radiation may be taken into consideration in interpreting the PC values derived by the procedures presented here. If it is believed that some other risk factor operates additively with radiation, and the individual is thought to have been exposed to that risk factor to an extent greater than the average for the population generally, then the PC obtained from the present procedures·may be somewhat excessive. But if it is believed that the second risk factor may combine with radiation to enhance risk in multiplicative fashion, the PC estimates based on these procedures should be unbiassed.

The procedures for calculating PC values for the pancreas are based on the principles and assumptions of Chapter V and the procedures of Chapters VI and IX. As with most sites, for cancer of the pancreas the relative excess, R, in the basic equation

$$PC = R/(1 + R)$$

is found as the product of three functions, i.e.,

$$R = F(D) \times T(Y) \times K(A_1,S)$$

where F(D) represents the influence of the low-LET tissue dose (D), T(Y) represents the variation in R over time in years (Y) after exposure, and $K(A_1,S)$ represents the relative excess of pancreatic cancer for a person of age A_1 and sex S, when both F and T = 1.

Under the linear-quadratic dose-response model assumed for pancreatic cancer, when exposure is to low-LET radiation

$$F = D + D^2/116.$$

For cancer of the pancreas the influence of time (T) on the relative risk depends entirely on years from exposure to diagnosis (Y). The function T is tabled below:

Y	0-4	5	6	7	8	9	10+
T	0	.074	.259	.500	.741	.926	1.

The standardized relative risk of excess cancer of the pancreas, K, is given in the accompanying Table X-8 for low-LET radiation exposure in rad and for each sex and age in completed years from 20 to 75.

A few examples may clarify the actual computational procedures for pancreatic cancer following exposure to ionizing radiation.

Example 1   A typical female, exposed at age 35 to 10 rad of low-LET radiation to the pancreas, with diagnosis at age 50. Then D = 10, A_1 = 35, and Y = 15.

$$F(D) = 10 + 10^2/116 = 10.86$$

$$T(Y) = T(15) = 1$$

$$K (A_1, S) = K(35, f) = .00184$$

$$\text{then } R = F \times T \times K = 10.86 \times 1 \times .00184 = .020$$

$$\text{and } PC = R/(1 + R) = .020/1.020 = .0196 \text{ or } 2\%.$$

Example 2   A typical male, exposed to 5 rad of low-LET radiation to the pancreas at age 40, with a diagnosis at age 51, 11 years after exposure. Then D = 5, A_1 = 40, and Y = 11.

$$F(5) = 5 + 5^2/116 = 5.22$$

$$T(11) = 1$$

$$K(40, m) = .000933$$

$$\text{then } R = F \times T \times K = 5.22 \times 1 \times .000933 = .00487$$

$$\text{and } PC = R/(1 + R) = .00487/1.00487 = .0049 \text{ or less than } 1\%.$$

Example 3 A pancreatic cancer was diagnosed at age 44 in a woman following several exposures to low-LET radiation at various ages. The first, of one rad to the pancreas, occurred at age 20, 24 years and 2 months before diagnosis (Y = 24). The second, to 2 rad, occurred 4 months later, at the same age (A_1 = 20) but 23 years and 10 months before diagnosis (Y = 23). At age 21, 23 years and 3 months before diagnosis, a 9-rad total dose was received over a 36-hour period at the continuous rate of 250 milli-rad per hour (Y = 23). Finally, at age 35, three exposures, to 1.1, 0.6, and 0.7 rad, respectively, were received on consecutive days, 9 years and 2 months prior to diagnosis (Y = 9).

The first, second, and third exposures should be considered separately, because exposures 1 and 2 correspond to different values of Y, and exposures 2 and 3 to different exposure ages. The 9-rad continuous exposure delivered over 36 hours should be treated as 2 exposures because it required more than one day, but less than two. The suggested partition assigns a 3-rad exposure to one 24-hour period and 6 rad to another. The three exposures at age 35 can be treated as one because they correspond to the same values of A_1 and Y, and because the total dose is less than 5 rad.

Exposure 1:

$$F(D) = 1 + 1^2/116 = 1.01$$

$$T(Y) = T(24) = 1$$

$$K(20,f) = .00739$$

$$R_1 = F \times T \times K = 1.01 \times 1 \times .00739 = .00746$$

Exposure 2:

$$F(2) = 2 + 2^2/116 = 2.03$$

$$T(23) = 1$$

$$K(20,f) = .00739$$

$$R_2 = F \times T \times K = 2.03 \times 1 \times .00739 = .0150$$

Exposure 3a:

$$F(3) = 3 + 3^2/116 = 3.08$$

$$T(23) = 1$$

$$K(21,f) = .00664$$

$$R_{3a} = F \times T \times K = 3.08 \times 1 \times .00664 = .0204$$

Exposure 3b:

$$F(6) = 6 + 6^2/116 = 6.31$$

$$T(23) = 1$$

$$K(21,f) = .00664$$

$$R_{3b} = F \times T \times K = 6.31 \times 1 \times .00664 = .0419$$

Exposures 4, 5, and 6:

$$F(1.1 + 0.6 + 0.7) = F(2.4) = 2.4 + 2.4^2/116 = 2.45$$

$$T(9) = .926$$

$$K(35,f) = .00184$$

$$R_{4,5,6} = F \times T \times K = 2.45 = .926 \times .00184 = .00417$$

$$R = R_1 + R_2 + R_{3a} + R_{3b} + R_{4,5,6} = .00746$$

$$+ .0150 + .0204 + .0419 + .00417 = .089$$

$$PC = R/(1 + R) = .089/1.089 = .082 = 8\%.$$

The uncertainty surrounding PC estimates is discussed in Chapter VII, and Section VII-O includes a derivation of approximate 90 percent credibility intervals for PC estimates.

To provide a general orientation to the magnitude of the PC values that result from the procedures described here, Fig. X-8 has been prepared for pancreatic cancer. It gives PC values for 1, 10, and 100 rad of low-LET radiation to pancreatic tissue by age at diagnosis, separately for males and females. The vertical scale is logarithmic and curves are presented for only two radiation dose levels. For these and other reasons interpolation is to be discouraged.

Fig. X-8
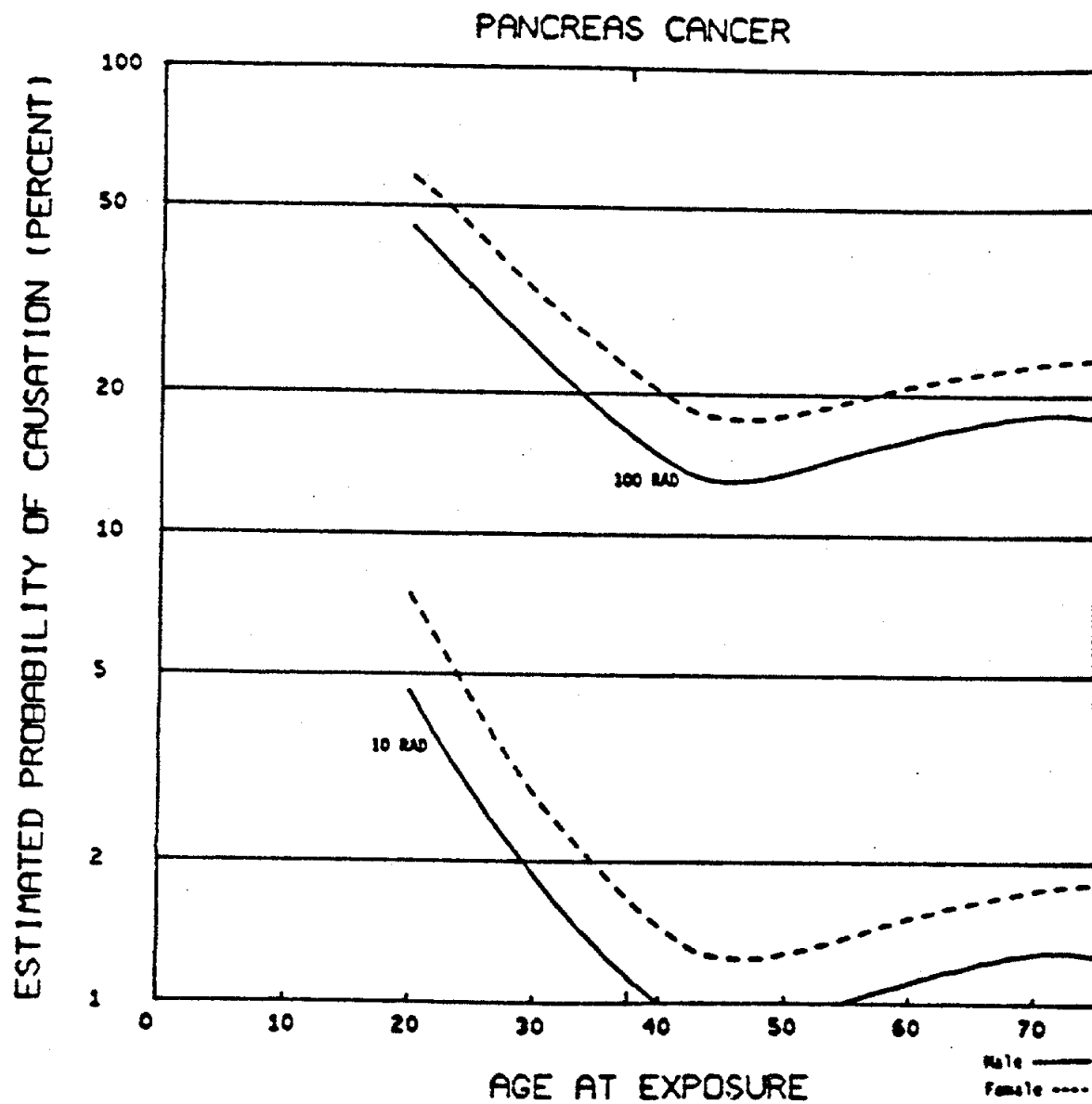
PANCREAS CANCER

Table X-8. Pancreas Cancer: Relative Excess $K(A_1, S)$ by Exposure Age A_1 and Sex S

A_1	Sex		A_1	Sex	
	Male	Female		Male	Female
20	.00446	.00739	48	.000821	.00117
21	.00400	.00664	49	.000832	.00118
22	.00360	.00596	50	.000846	.00119
23	.00325	.00534	51	.000863	.00121
24	.00295	.00478	52	.000881	.00123
25	.00269	.00429	53	.000901	.00125
26	.00246	.00386	54	.000921	.00127
27	.00226	.00349	55	.000940	.00129
28	.00208	.00317	56	.000960	.00132
29	.00191	.00289	57	.000979	.00134
30	.00176	.00265	58	.000998	.00137
31	.00163	.00245	59	.00102	.00140
32	.00151	.00227	60	.00103	.00142
33	.00141	.00211	61	.00105	.00145
34	.00131	.00197	62	.00107	.00147
35	.00123	.00184	63	.00109	.00149
36	.00116	.00172	64	.00111	.00151
37	.00109	.00162	65	.00112	.00153
38	.00103	.00152	66	.00114	.00155
39	.000980	.00144	67	.00116	.00158
40	.000933	.00136	68	.00117	.00160
41	.000891	.00130	69	.00119	.00162
42	.000855	.00124	70	.00120	.00164
43	.000831	.00121	71	.00120	.00165
44	.000817	.00118	72	.00120	.00166
45	.000810	.00117	73	.00120	.00168
46	.000809	.00116	74	.00119	.00168
47	.000813	.00116	75	.00118	.00169

9. Lung Cancer (162.1 in ICDA-8)

Introduction

The association between ionizing radiation and cancer of the lung and bronchus has been most clearly evident in various studies of underground miners who are exposed to radon and its daughter products (48-50). The results of the studies on miners are broadly consistent with other studies of the relation of X rays and gamma rays to respiratory cancer, notably those of the Japanese A-bomb survivors (28) and the British ankylosing spondylitis patients who were treated with X rays (3).

The BEIR III assessment of lung cancer risk following exposure to ionizing radiation was a synthesis of epidemiologic data from a number of studies of mining populations with occupational exposure to alpha radiation from inhaled radon daughters, and from the Japanese A-bomb survivor studies and the British series of patients given X-ray therapy for ankylosing spondylitis, both representing exposure to external, mainly low-LET, radiation. In that assessment it was concluded that, among miners, excess lung cancer risk was proportional to cumulative exposure to radon daughters, measured in "working level months" (WLM), and that excess risk was proportional to cumulative dose from low-LET radiation, with approximate equivalance of effect between one WLM and 6 rad low-LET dose to the bronchial epithelium. (One "working level" (WL) is defined as the activity in air that gives 13,000 MeV of alpha radiation per liter from ultimate decay of the short-lived daughters; one WLM is defined as exposure to 1 WL for 170 hours.) In the BEIR assessment, age at observation was a far more important determinant of excess risk than age at exposure. For a given cumulative exposure, and after a minimum latent period, estimated risk increased approximately linearly with age at observation, from zero before age 35 to a maximal value at about age 70 and older (4, pp. 198, 325-327).

The Working Group found the BEIR analysis difficult to use, partly because the formula of a linear increase in excess risk with increasing age at observation is inconsistent with the constant relative risk model for time from exposure to diagnosis, a model that the A-bomb survivor lung cancer mortality data for 1950-1978 appear to support (28,33). Also, there is some evidence that the two kinds of radiation may differ in their carcinogenic effects. The shape of the dose-response relationship is probably different for the two types of radiation (see Chapters III-1 and V-B). Moreover, the A-bomb survivor data strongly suggest an additive relationship between exposure to low-LET radiation and smoking in the causation of lung cancer (51), whereas the relevant data for radon daughter exposure and smoking, while mixed (52-54), tend, on the whole, to suggest a multiplicative interaction model (49,55-59). It was also noted that there is no real necessity to base risk estimates on the combined data from the two kinds of exposure; there are sufficient data to support separate lung cancer risk analyses for external, low-LET radiation and exposure to inhaled radon daughter products.

Estimates for high-LET radiation

The many studies of lung cancer risk in mining populations exposed to

radon daughter products are remarkable for the diversity of risk estimates produced. Estimates based on reasonably large mining populations range from 0.3 percent relative excess per WLM for U.S. uranium miners (59) to 3 percent or more in Swedish metal miners and Canadian uranium miners (55). Reviews of the mining population data have tended to differ in the amount of weight given to the various studies. In a recent proportional hazard model analysis of data from Czech, U.S., and Canadian uranium miners, Jacobi et al. obtained estimates of, respectively, 1.5, 0.7 and (about) 1.5 percent relative excess risk per WLM with a weighted average of 1.2 percent per WLM (60). Another review, by Thomas and McNeill, placed less weight on the U.S. uranium miner data and, using a different analytical approach, obtained an overall estimate of 2.3 percent per WLM (55).

Another source of variability in studies and reviews by expert committees is the assumed distribution of excess risk over time following exposure. Lundin et al. (61) postulated a lognormal model for time to response in their analysis of U.S. uranium miner data, while Whittemore and McMillan assumed a constant relative risk model in their analysis of substantially the same data (59). The authors of NCRP Report No. 78 (62) assumed a decreasing absolute risk model with a 20-year half-life for stem cells transformed by alpha radiation (63). Recently, Jacobi et al. introduced a proportional hazards model, incorporating the constant relative risk model (60). Previously, Jacobi and the ICRP had employed the constant absolute risk model (64,65). Ellett and Nelson (66) have used lung cancer data from smoking and non-smoking iron miners in Sweden to test various time-to-response models for lung cancer induced by exposure to radon daughters. Their analysis found that the constant relative risk model gave a reasonably good fit to the observed age-at-diagnosis data, whereas the BEIR model gave a marginally unsatisfactory fit; the constant absolute risk model and the decreasing absolute risk model of NCRP Report No. 78, on the other hand, deviated markedly from these data.

Expert committees of the ICRP and the U.S. National Academy of Sciences are now preparing, or will soon prepare, assessments of lung cancer risk associated with exposure to radon daughters. In the meantime, there is no one "official" estimate that appears to take precedence over all others. The estimate most nearly consistent with the approach of the present Working Group is that calculated by Jacobi et al. (60); according to that estimate, the relative excess risk R associated with a single exposure of reasonably short duration, measured in WLM, might be calculated as

$$R = U \times T(Y) \times 1.2 \text{ percent per WLM}$$

where U is the exposure in WLM, and the temporal factor $T(Y)$ is defined in the same way as for lung cancer following external, low-LET radiation. The method of estimating exposure for U.S. uranium miners prior to 1961 appears to have been different from that used after that date and those used in other countries, and is considered on the whole to have over-estimated exposure (55,61). There is, therefore, some justification for using a different risk factor for U.S. miner exposures before 1961, such as the value of 0.7% per WLM estimated by Jacobi et al. (60). Because

the U.S. data for exposures before 1961 are included in the weighted
average calculated by Jacobi, there is also reason to use a higher risk
factor, such as the value 1.5 percent per WLM calculated from Czech and
Canadian data (60), for later exposures. The Working Group wishes to empha-
size, however, that the range of published risk estimates is somewhat greater
than from 0.7 to 1.5 percent per WLM, and that reviews by expert committees
may provide us with different estimates within the next year or so.

One marked difference between the above algorithm and that recommended
below for low-LET radiation is that in the above expression relative excess
does not depend upon age at exposure. In fact, age at exposure is difficult
to study in mining populations because exposure tends to be spread out
over many years. Moreover, given the uncertainty of age-specific risk
coefficients derived from the A-bomb survivor data, it is entirely possible
that, over the age ranges at which most mining exposures are received,
there is little variation in susceptibility by age at exposure.

Another difference is that, for alpha radiation from inhaled radon
daughter products, a multiplicative interaction is assumed to hold with
respect to smoking. Thus, unlike the algorithm for external, low-LET
radiation, the relative excess is invariant under differences in smoking
level.

Estimates for low-LET radiation

Estimates based on the A-bomb survivor series and the British
spondylitis series are in good agreement (67). Accordingly, new risk
coefficients were calculated for low-LET radiation, based on the A-bomb
survivor lung cancer mortality data for 1955-1978 (28). Regression
coefficients calculated separately for exposure ages 10-19, 20-34, 35-49,
and 50+ conformed to a roughly linear pattern of dependence on exposure
age; the absolute risk coefficients in Table VI-1, and the coefficients
for relative excess in Table X-9-A therefore incorporate a linear
dependence on age at exposure, plus a correction for an estimated 30
percent underascertainment from death certificates. This correction allows
for some improvement in ascertainment efficiency since the report of
Steer et al., which was largely based on autopsy and death certificate
data from the 1960s (68).

Lung cancer is not one of the cancers reliably identified by those
who fill out death certificates, but the errors are mostly in the
direction of under-reporting primary cancer of the lung and bronchus.

The NCI SEER data on the incidence of lung cancer in the US by age
and sex, for the years 1973-1981, are used for the normal risk of lung
cancer in calculating PC values for low-LET radiation. As may be seen in
Tables VII-1 and VII-2, the SEER reporting areas differ considerably in
their reported baseline levels of incidence (the range is 42 to 113 for
males) (8). Although the main risk factor for lung cancer is smoking,
for which adjustments can be made as discussed in Chapter IV, Section H,
and in Chapter IX, there are other important etiologic agents that may
pose difficulties, notably asbestos, polycyclic hydrocarbons, chloromethyl
ethers, chromium, nickel, and inorganic arsenic (69). As noted in Chapter
IV-G and in Chapter IX, risk co-factors other than smoking may be taken

into consideration in interpreting the PC values derived by the procedures presented here. If it is believed that some other risk factor operates additively with radiation, and the individual is thought to have been exposed to that risk factor to an extent greater than the average for the population generally, then the PC obtained from the present procedures may be somewhat excessive. But if it is believed that the second risk factor may combine with radiation to enhance risk in multiplicative fashion, the PC estimates based on these procedures should be unbiassed.

For lung cancer, the relative excess, R, in the basic equation

$$PC = R/(1 + R)$$

is found as the product of three functions, i.e.,

$$R = F(D) \times T(Y) \times K(A_1, S)$$

where $F(D)$ represents the contribution of the low-LET tissue dose (D) in rad, $T(Y)$ represents the variation in R over time in years (Y) after exposure, and $K(A_1, S)$ represents the relative excess risk of lung cancer for a person of sex S and age A_1 at exposure, when both F and T = 1.

Under the linear-quadratic model assumed for the lung when exposure is to low-LET radiation,

$$F = D + D^2/116.$$

For the lung, the influence of time (T) on the relative risk depends only on years from exposure to diagnosis (Y).

Y	0-4	5	6	7	8	9	10+
T	0	.074	.259	.500	.741	.926	1

The standardized relative risk of excess lung cancer, K, is given in the accompanying Table X-9-A for low-LET radiation and for each sex and completed year of age at exposure from 10 to 75.

Because cigarette smoking dominates the risk of lung cancer in the general population, the PC estimate should, if possible, take smoking history into account. As explained in Chapter IV, the multiplicative interaction model would require no adjustment for smoking history, but the additive interaction model seems more appropriate for lung cancer, at least for low-LET radiation. This requires that the influence of smoking history be incorporated into the expression for R when calculating PC's. This results in a multiplier for R, calculated as the average population risk divided by the average risk in the relevant smoking category. This ratio is W in the Chapter IV discussion, and the values developed there are repeated in Table X-9-B. Then the value of R, modified to show the influence of smoking status, becomes

$$R = F \times T \times K \times W.$$

A few examples should make it clear how the PC values are to be obtained for individual cases:

Example 1   A non-smoking male, exposed to 5 rad of low-LET radiation to the lung at age 20, with a diagnosis at age 50, otherwise typical of his age-sex group with respect to the risk of lung cancer.   Then $D = 5$, $A_1 = 20$, $Y = 30$, and $W = 6.81$

$$F(D) = 5 + 5^2/116 = 5.22$$

$$T(Y) = T(30) = 1$$

$$K(A_1,S) = K(20,m) = .00122$$

$$W = 6.81$$

$$\text{then } R = F \times T \times K \times W = 5.22 \times 1 \times .00122 \times 6.81 = .0434$$

$$\text{and } PC = R/(1 + R) = .0434/1.0434 = .042 \text{ or } 4\%.$$

Example 2   A lung cancer was diagnosed at age 44 in a non-smoking woman following several exposures to low-LET radiation at various ages.   The first, of one rad to the lung, occurred at age 20, 24 years and 2 months before diagnosis ($Y = 24$).   The second, to 2 rad, occurred 4 months later, at the same age ($A_1 = 20$) but 23 years and 10 months before diagnosis ($Y = 23$).   At age 21, 23 years and 3 months before diagnosis, a 9 rad total dose was received over a 36-hour period at the continuous rate of 250 millirad per hour ($Y = 23$).   Finally, at age 35, three exposures, to 1.1, 0.6, and 0.7 rad, respectively, were received on consecutive days, 9 years and 2 months prior to diagnosis ($Y = 9$).   For a non-smoking female $W = 4.64$.

The first, second, and third exposures should be considered separately, because exposures 1 and 2 correspond to different values of Y, and exposures 2 and 3 to different exposure ages.   The 9-rad continuous exposure delivered over 36 hours should be treated as 2 exposures because it required more than one day, but less than two.   The partition giving the maximum risk estimate assigns a 3-rad exposure to one 24-hour period and 6 rad to another.   The three exposures at age 35 can be treated as one because they correspond to the same values of A_1 and Y, and because the total dose is less than 5 rad.

Exposure 1:

$$F(D) = F(1) = 1 + 1^2/116 = 1.01$$

$$T(Y) = T(24) = 1$$

$$K(A_1,S) = K(20,f) = .00230$$

$$R_1 = F \times T \times K \times W = 1.01 \times 1 \times .00230 \times 4.64 = .0108$$

Exposure 2:

$$F(2) = 2 + 2^2/116 = 2.03$$

$T(23) = 1$

$K(20,f) = .00230$

$R_2 - F \times T \times K \times W = 2.03 \times 1 \times .00230 \times 4.64 = .0217$

Exposure 3a:

$F(3) = 3 + 3^2/116 = 3.08$

$T(23) = 1$

$K(21,f) = .00214$

$R_{3a} = F \times T \times K \times W = 3.08 \times 1 \times .00214 \times 4.64 = .0306$

Exposure 3b:

$F(6) = 6 + 6^2/116 = 6.31$

$T(23) = 1$

$K(21,f) = .00214$

$R_{3b} = F \times T \times K \times W = 6.31 \times 1 \times .00214 \times 4.64 = .0627$

Exposures 4, 5 and 6:

$F(1.1 + 0.6 + 0.7) = F(2.4) = 2.4 + 2.4^2/116 = 2.45$

$T(9) = .926$

$K(35,f) = .00104$

$R_{4,5,6} = F \times T \times K \times W = 2.45 \times .926 \times .00104 \times 4.64 = .0109$

$R = R_1 + R_2 + R_{3a} + R_{3b} + R_{4,5,6} =$

$+ .0108 + .0217 + .0306 + .0627 + .0109 = .1367$

$PC = R/(1 + R) = .1367/1.1367 = .120$ or 12%.

Example 3 A lung cancer was diagnosed in a man whose only known radiation exposure was to inhaled radon and radon daughters while employed as a uranium miner during the period 1950-1968. The most recent exposure occurred more than 10 years before diagnosis. Total recorded exposure was to 140 WLM, of which 100 WLM was before 1961 and 40 WLM afterward. If the risk factor .012 per WLM is applied to the total exposure, the calculated relative excess is

$R = 140 \times .012 = 1.68$

and the PC is

$$PC = R/(1 + R) = 1.68/2.68 = .626 = 63\%.$$

The same result is obtained by looking up in Table PC-9-I (Appendix I) the PC for 140 WLM with an assumed excess risk of 1.2%. However, it may be desirable to use different relative excess risks because of employment as a miner both before and after 1961. In this case, Table PC-9-I cannot be used and calculations are as follows:

If the factor .007 is applied to exposures before 1961 and the factor .015 to exposures afterward, the relative excess is

$$R = 100 \times .007 + 40 \times .015 = 1.30,$$

and the PC is

$$PC = 1.30/2.30 = .565 = 57\%.$$

The uncertainty surrounding PC estimates is discussed in Chapter VII, and Section VII-O includes a derivation of approximate 90 percent credibility intervals for PC estimates.

To provide an orientation to the general magnitude of the PC values that result from the procedures described here, Fig X-9 has been drawn for tissue doses of 1, 10, and 100 rad of low-LET radiation, and PC values plotted by age at exposure, for both males and females, on the assumption that the minimal latent period has been satisfied and with no information with respect to smoking history. The vertical scale is logarithmic and curves are presented for only three radiation dose levels. For these and other reasons interpolation is to be discouraged.

Fig X-9
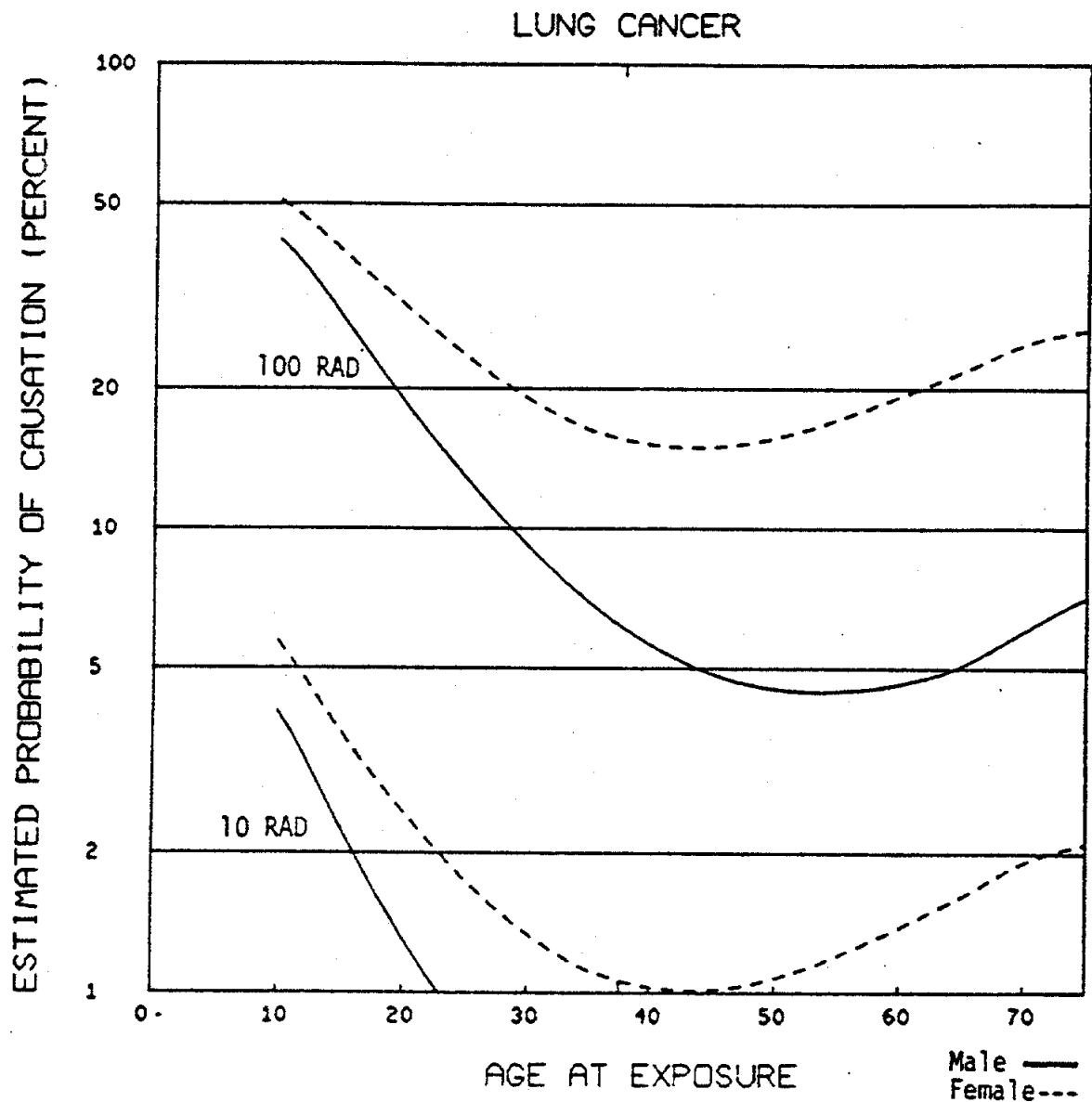
LUNG CANCER

Table X-9-A   Lung Cancer: Relative Excess K(A ,S)
    by Exposure Age A_1 and Sex S

A_1	Sex		A	Sex	
	Male	Female		Male	Female
10	.00387	.00557	43	.000288	.000942
11	.00349	.00510	44	.000280	.000942
12	.00311	.00465	45	.000274	.000945
13	.00275	.00422	46	.000268	.000950
14	.00243	.00383	47	.000263	.000959
15	.00214	.00349	48	.000260	.000970
16	.00190	.00318	49	.000256	.000985
17	.00169	.00292	50	.000254	.00100
18	.00151	.00269	51	.000252	.00102
19	.00136	.00248	52	.000251	.00104
20	.00122	.00230	53	.000250	.00106
21	.00111	.00214	54	.000250	.00109
22	.00101	.00199	55	.000251	.00112
23	.000925	.00186	56	.000252	.00115
24	.000849	.00174	57	.000253	.00118
25	.000781	.00163	58	.000255	.00122
26	.000721	.00154	59	.000258	.00125
27	.000667	.00145	60	.000261	.00129
28	.000619	.00138	61	.000265	.00133
29	.000576	.00131	62	.000269	.00137
30	.000537	.00125	63	.000274	.00142
31	.000503	.00120	64	.000280	.00146
32	.000472	.00115	65	.000288	.00151
33	.000444	.00111	66	.000297	.00156
34	.000419	.00107	67	.000308	.00162
35	.000397	.00104	68	.000319	.00168
36	.000377	.00102	69	.000331	.00174
37	.000359	.000998	70	.000344	.00179
38	.000344	.000981	71	.000357	.00184
39	.000330	.000968	72	.000370	.00188
40	.000318	.000957	73	.000384	.00191
41	.000307	.000950	74	.000398	.00194
42	.000297	.000945	75	.000411	.00197

Table X-9-B

W, The Factor Used To Adjust Average
Population Incidence for Smoking History

Smoking Category	W	
	Males	Females
Total	1.00	1.00
Nonsmokers	6.81	4.64
Former smokers	1.71	1.17
Present cigarette smokers, all	0.604	0.412
under 10/day	1.75	1.19
10 - 20/day	0.707	0.482
21 - 39/day	0.408	0.278
40 +/day	0.287	0.196

10. <u>Cancer of the Female Breast</u>   (174 in ICDA-8)

Risk estimates for radiation-induced cancer of the female breast are the most secure for any site. The 1980 BEIR report was preceded by publication of incidence data on the Life Span Study sample of Japanese A-bomb survivors (70), former patients at Massachusetts tuberculosis sanitoria who received substantial cumulative breast doses from multiple fluoroscopic examinations (71), and women treated with X rays for acute postpartum mastitis (72). The estimates in the 1980 BEIR report were based on an analysis in parallel of data from these three sources (73,74).

A remarkable feature of the analysis in parallel was that similar estimates of the absolute magnitude of risk were obtained from the three samples for similar ages at exposure and lengths of follow-up, despite 3 to 5-fold differences in baseline risk between Japanese and US women (75). A possible interpretation of this finding is that factors in the American lifestyle responsible for the difference (American women of Japanese descent have breast cancer rates approaching those of other American women) are additive with radiation in the causation of breast cancer. The data also were highly consistent with proportionality between radiation dose and excess risk, and with the constant relative risk model for induction period.

Estimates for women exposed after age 40 were uncertain because the two medical series contained few relevant data and the A-bomb survivor data, which were consistent with little or no excess risk, suggested the possibility that a radiation effect on ovarian function might have reduced the risk of breast cancer among older women. Evidence for excess risk among Swedish women treated with X rays for benign breast disease (76) at ages above 40 seemed questionable because of the possibility that the excess might be attributable to the indication for treatment, e.g., chronic cystic mastitis, known to be a risk factor for breast cancer. This uncertainty was resolved by the BEIR committee at the time by applying risk coefficients for exposures at ages 20-39 to those at older ages, with the implicit understanding that this might overestimate risk from exposure after age 40.

At the time of the 1980 BEIR report no persuasive evidence of excess breast cancer risk in women irradiated before about age 10 had been presented, and while it seemed possible that an excess would appear when the youngest A-bomb survivors reached ages at which breast cancer normally reaches appreciable levels, it also seemed possible that lack of different-iated breast target tissue might preclude a carcinogenic effect of radiation. Further follow-up studies of A-bomb survivors (77,78) and American women treated in infancy for supposedly enlarged thymus gland (79) have shown that irradiation during early childhood does increase the risk of breast cancer, that this risk does not appear until after about age 30, when breast cancer rates normally increase, and that the excess, when it does appear, is comparable to that seen in women irradiated during their teens, previously considered to be the ages of greatest sensitivity. The two studies make it plain that the BEIR coefficient of 0 for women exposed under ten years of age is inappropriate and should be replaced. Moreover, the more recent study of A-bomb survivors (78) is based on a sufficiently large experience at the older ages to provide adequate estimates for

women aged 40 or older and these indicate that the flat projection of risk from age 20 in the BEIR report can no longer be supported. Accordingly, age-specific coefficients developed from that more recent study have been substituted for those given in the BEIR report (see Chapter V-D).

Other recent developments include a record-linkage study (80) of breast cancer mortality among some 110,000 Canadian women given multiple chest fluoroscopies during treatment at tuberculosis sanitoria in Canada. The radiation exposures were highly fractionated and delivered over periods of years. The data from this study were interpreted as suggestive of a strongly quadratic, rather than linear, dose response. This interpretation, which seems contradictory to the general observation from experimental radiobiology that fractionation and protraction of dose reduce nonlinear components of the dose response (81), appears to rest on a difference between data from Nova Scotia, where total doses tended to be high, and other Canadian provinces, where doses tended to be lower because patients usually were examined with their backs to the X-ray source. Considerable uncertainty surrounds the dosimetry data for the Canadian series, and it is of interest that the initial publication of a small Nova Scotia series (82), which employed incidence rather than mortality, suggested linearity of dose-response to the first BEIR committee (83).

Despite its general preference for the linear-quadratic dose-response function, the Working Group considered that all the data for breast cancer except those in the recent Canadian report were so strongly linear that it was important to make an exception of breast cancer and to assume linearity of dose-response in developing the PC estimation procedure for this site. The time-response data on breast cancer definitely point to the constant relative risk model as the basis for distributing excess cases over time, with a latent period (for incidence) of 10 years smoothed as described in Chapter V-C. Since the underlying data on breast cancer are extensive, are derived from numerous exposure situations, and are relatively non-controversial, PC estimates for this site are probably more reliable than for any other site. The general procedures for estimating PC values are described in Chapters VI and IX.

Breast cancer baseline rates vary somewhat by geographic region. Tables VII-1 and VII-2 illustrate the variability seen in the SEER data of the National Cancer Insitute from which the baseline or normal incidence data were taken (8). There are many risk factors for breast cancer in addition to exposure to ionizing radiation, especially early menarche, nulliparity, delayed age at first completed pregnancy, positive family history, and pre-existing proliferative breast disease (84). As noted in Chapter IV-G and in Chapter IX, risk factors other than ionizing radiation may be taken into consideration in interpreting the PC values derived by the procedures presented here. If it is believed that some other risk factor operates additively with radiation, and the individual is thought to have been exposed to that risk factor to an extent greater than the average for the population generally, then the PC obtained from the present procedures may be somewhat excessive. If it is believed that the second risk factor may combine with radiation to enhance risk in multiplicative fashion, the PC estimates based on these procedures should be unbiassed. For breast cancer the relative excess, R, in the basic equation

$$PC = R/(1 + R)$$

is found as the product of three functions, i.e.,

$$R = F(D) \times T(Y) \times K(A_1)$$

where $F(D)$ represents the influence of the low-LET tissue dose (D), $T(Y)$ represents the variation in R over time in years (Y) after exposure, and $K(A_1)$ represents the relative excess risk of breast cancer for a woman of age A_1 at exposure, when both F and T = 1.

Under the linear model assumed for breast cancer, $F = D$ for low-LET radiation.

For breast cancer the influence of time (T) on the relative risk does not vary by age at exposure but does depend on years from exposure to diagnosis (Y) in the following fashion:

Y	0-4	5	6	7	8	9	10+
T	0	.074	.259	.500	.741	.926	1

The standardized relative risk of excess breast cancer, K, is given in the accompanying Table X-10 for low-LET radiation and for each completed year of age from birth to 75.

A few examples should illustrate how the PC values are to be obtained in individual cases.

Example 1   A typical female, aged 10 when exposed to 10 rad of low-LET radiation to breast tissue, with a diagnosis of breast cancer at age 35. That is, $D = 10$, $A_1 = 10$, and $Y = 25$.

$$F(D) = 10$$

$$T(Y) = T(25) = 1$$

$$K(A_1,S) = K(10) = .0144$$

$$\text{then } R = 10 \times 1 \times .0144 = .144$$

$$\text{and } PC = R/(1 + R) = .144/1.144 = .126 \text{ or } 13\%.$$

Example 2   A breast cancer was diagnosed at age 44 in a woman following several exposures to low-LET radiation at various ages. The first, of one rad to the breast in which cancer was later diagnosed, occurred at age 20, 24 years and 2 months before diagnosis (Y = 24). The second, to 2 rad, occurred 4 months later, at the same age (A_1=20) but 23 years and 10 months before diagnosis (Y = 23). At age 21, 23 years and 3 months before diagnosis, a 9-rad total dose was received over a 36-hour period at the continuous rate of 250 millirad per hour (Y = 23). Finally, at age 35, three exposures, to 1.1, 0.6, and 0.7 rad, respectively, were received on consecutive days, 9 years and 2 months prior to diagnosis (Y = 9).

The first, second, and third exposures should be considered separately because exposures 1 and 2 correspond to different values of Y, and exposures 2 and 3 to different exposure ages. The 9-rad continuous exposure delivered over 36 hours can be treated as a single exposure because estimated risk under the linear model depends only upon the total dose. Similarly, the three exposures at age 35 can be treated as a single exposure.

Exposure 1:

$$F(D) = F(1) = 1$$

$$T(Y) = T(24) = 1$$

$$K(A_1,S) = K(20,f) = .00606$$

$$R_1 = F \times T \times K = 1 \times 1 \times .00606 = .00606$$

Exposure 2:

$$F(2) = 2$$

$$T(23) = 1$$

$$K(20,f) = .00606$$

$$R_2 = F \times T \times K = 2 \times 1 \times .00606 = .0121$$

Exposure 3:

$$F(9) = 9$$

$$T(23) = 1$$

$$K(21,f) = .00523$$

$$R_3 = F \times T \times K = 9 \times 1 \times .00523 = .0471$$

Exposures 4, 5, and 6:

$$F(1.1 + 0.6 + 0.7) = F(2.4) = 2.4$$

$$T(9) = .926$$

$$K(35,f) = .00214$$

$$R_{4,5,6} = F \times T \times K = 2.4 \times .926 \times .00214 = .00476$$

$$R = R_1 + R_2 + R_3 + R_{4,5,6} = .00606 + .0121 + .0471$$
$$+ .00476 = .0700$$

$$PC = R/(1 + R) = .0700/1.0700 = .0654 \text{ or } 7\%.$$

The uncertainty surrounding PC estimates is discussed in Chapter VII, and Section VII-0 includes a derivation of approximate 90 percent credibility intervals for PC estimates.

To provide an orientation to the general magnitude of the PC values that result from the procedures described here, Fig X-10 has been drawn for tissue doses of 1, 10, and 100 rad of low-LET radiation, and PC values plotted by age at exposure and on the assumption that the minimal latent period has been satisfied. The vertical scale is logarithmic and curves are presented for only three radiation dose levels. For these and other reasons interpolation is to be discouraged.

Fig. X-10
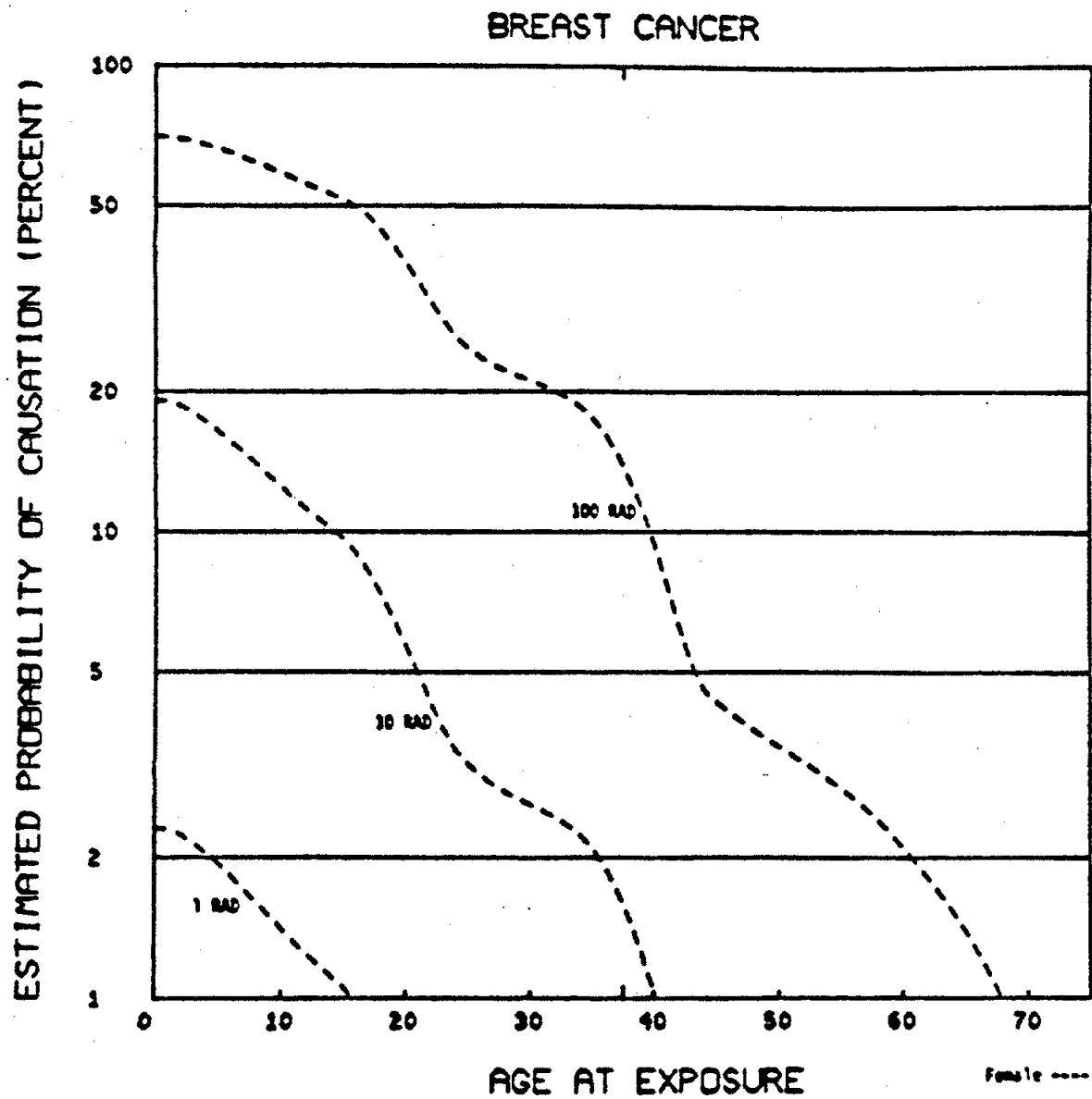
BREAST CANCER

Table X-10.   Female Breast Cancer: Relative Excess
   K(A₁,S) by Exposure Age A₁

A_1	Sex		A_1	Sex	
	Male	Female		Male	Female
0	---	.0237	38	---	.00150
1	---	.0236	39	---	.00126
2	---	.0230	40	---	.00104
3	---	.0220	41	---	.000835
4	---	.0209	42	---	.000669
5	---	.0198	43	---	.000547
6	---	.0186	44	---	.000478
7	---	.0174	45	---	.000452
8	---	.0163	46	---	.000429
9	---	.0153	47	---	.000409
10	---	.0144	48	---	.000391
11	---	.0134	49	---	.000375
12	---	.0126	50	---	.000359
13	---	.0119	51	---	.000345
14	---	.0113	52	---	.000331
15	---	.0107	53	---	.000318
16	---	.00992	54	---	.000305
17	---	.00897	55	---	.000291
18	---	.00797	56	---	.000277
19	---	.00699	57	---	.000263
20	---	.00606	58	---	.000248
21	---	.00523	59	---	.000231
22	---	.00452	60	---	.000215
23	---	.00395	61	---	.000200
24	---	.00354	62	---	.000185
25	---	.00329	63	---	.000170
26	---	.00310	64	---	.000155
27	---	.00296	65	---	.000141
28	---	.00285	66	---	.000127
29	---	.00276	67	---	.000113
30	---	.00268	68	---	.0000996
31	---	.00260	69	---	.0000859
32	---	.00251	70	---	.0000720
33	---	.00241	71	---	.0000580
34	---	.00229	72	---	.0000437
35	---	.00214	73	---	.0000293
36	---	.00195	74	---	.0000148
37	---	.00173	75	---	0

11. Cancer of Kidney or Bladder   (188, 189.0, 189.1 in ICDA-8)

   Sensitivity to the carcinogenic effect of ionizing radiation is considered to be relatively low for both the kidney and the urinary bladder. Reported dose-specific risks are seldom high and in some studies no excess cancers have been found. Malignant tumors of the kidney, of the bladder, or of the undifferentiated "urinary organs" have been reported to be increased in frequency among the A-bomb survivors, persons treated with irradiation of the spine for ankylosing spondylitis, persons who received injections of Thorotrast in retrograde pyelography, and persons with cervical cancer treated by radiation (4,23). In some studies the relationship with radiation dose is uncertain or simply not demonstrable, and the data from the cervical cancer series are especially inconclusive (5). The strongest relationship is seen in the mortality experience of the A-bomb survivors over the period 1950-1978 (28), especially since it appears within each sex and within each city, but death certificate diagnoses are much less reliable for these sites than for many others.

   The BEIR III coefficients, adjusted to the period 11-30 years after exposure, have been used in the PC calculations as described in Chapters VI and IX, except that estimates were not made for those under age 20 at exposure for the reasons given in Chapter VII-F.

   The normal or baseline risk of cancers of the kidney and bladder has been taken from the data bank of the SEER program of the National Cancer Institute (8). The rates are for the period 1973-1981, for all races combined, and for all reporting areas combined except Puerto Rico. There is appreciable geographic variation within the US (see Tables VII-1 and VII-2) that apparently rests on differentials in industrial exposures that are of major importance for cancer of the bladder (85). Exposure to dyestuffs, rubber, leather, and certain organic chemicals has been associated with excess cancer of the bladder (86). An association between cigarette consumption and bladder cancer is well documented, and there is some evidence of an association with cancer of the kidney (85). As noted in Chapter IV-G and in Chapter IX, risk factors other than ionizing radiation may be taken into consideration in interpreting the PC values derived by the procedures presented here. If it is believed that some other risk factor operates additively with radiation, and the individual is thought to have been exposed to that risk factor to an extent greater than the average for the population generally, then the PC obtained from the present procedures may be somewhat excessive. But if it is believed that the second risk factor may combine with radiation to enhance risk in multiplicative fashion, the PC estimates based on these procedures should be unbiassed.

   The Working Group had no information available to it concerning the most appropriate dose-response function for cancers of the kidney and bladder, or the most suitable time-response function, or whether radiation may interact with other risk factors in multiplicative or additive fashion. It chose, therefore, to employ the preferred linear-quadratic model of dose-response, with no threshold, and the constant relative risk model for distributing excess cancers over time. The minimum latent period was taken as 10 years but smoothed as described in Chapter V-C.

The procedures for calculating PC values for cancers of the kidney and bladder are based on the assumptions and principles discussed in Chapter V and the procedures of Chapter VI and IX. As with most sites, for cancers of the kidney and bladder the relative excess, R, in the basic equation

$$PC = R/(1 + R)$$

is found as the product of three functions, i.e.,

$$R = F(D) \times T(Y) \times K(A_1,S)$$

where F(D) represents the influence of the low-LET tissue dose (D), T(Y) represents variation in R over time in years (Y) after exposure, while $K(A_1,S)$ represents the relative excess risk of cancer of the kidney or bladder for a person of age at exposure A_1 and sex S, when both F and T = 1.

Under the linear-quadratic model assumed for cancers of the kidney and bladder, when exposure is to low-LET radiation

$$F = D + D^2/116.$$

For cancers of the kidney and bladder the influence of time (T) on the relative risk depends entirely on years from exposure to diagnosis (Y). The function T is tabled below:

Y	0-4	5	6	7	8	9	10+
T	0	.074	.259	.500	.741	.926	1.

The standardized relative excess risk for cancer of the kidney or bladder, K, is given in the accompanying Table X-11 for low-LET radiation and for each sex and year of age (completed years) from 20 to 75.

A few examples should clarify the actual computational procedures for cancers of the kidney and bladder following exposure to ionizing radiation.

Example 1 A typical female, aged 35 when exposed to 10 rad of low-LET radiation to bladder tissue with diagnosis at age 55, 20 years after exposure. Then D = 10, A_1 = 35, and Y = 20

$$F(D) = 10 + 10^2/116 = 10.86$$

$$T(Y) = T(20) = 1$$

$$K(A_1,S) = K(35, f) = .00142$$

$$R = F \times T \times K = 10.86 \times 1 \times .00142 = .01542$$

and PC = .0154/1.0154 = .015 or 2%.

Example 2 A typical male, aged 55 at exposure to 5 rad of low-LET radiation to the kidney, with diagnosis at age 60, 4.9 years after exposure. That is, $D = 5$, $A_1 = 55$, and $Y = 4$.

$$F = 5 + 5^2/116 = 5.22$$

$$T(4) = 0$$

$$K(55,m) = .000275$$

$$\text{then } R = F \times T \times K = 5.22 \times 0 \times .000275 = 0$$

$$\text{and } PC = 0$$

Example 3 A kidney cancer was diagnosed at age 44 in a woman following several exposures to low-LET radiation at various ages. The first, of one rad to the kidney, occurred at age 20, 24 years and 2 months before diagnosis ($Y = 24$). The second, to 2 rad, occurred 4 months later, at the same age ($A_1 = 20$) but 23 years and 10 months before diagnosis ($Y = 23$). At age 21, 23 years and 3 months before diagnosis, a 9-rad total dose was received over a 36-hour period at the continuous rate of 250 millirad per hour ($Y = 23$). Finally, at age 35, three exposures, to 1.1, 0.6, and 0.7 rad, respectively, were received on consecutive days, 9 years and 2 months prior to diagnosis ($Y = 9$).

The first, second, and third exposures should be considered separately, because exposures 1 and 2 correspond to different values of Y, and exposures 2 and 3 to different exposure ages. The 9-rad continuous exposure delivered over 36 hours should be treated as 2 exposures because it required more than one day, but less than two. The suggested partition assigns a 3-rad exposure to one 24-hour period and 6 rad to another. The three exposures at age 35 can be treated as one because they correspond to the same values of Al and Y, and because the total dose is less than 5 rad.

Exposure 1:

$$F(D) = F(1) = 1 + 1^2/116 = 1.01$$

$$T(Y) = T(24) = 1$$

$$K(20,f) = .00301$$

$$R_1 = F \times T \times K = 1.01 \times 1 \times .00301 = .00304$$

Exposure 2:

$$F(2) = 2 + 2^2/116 = 2.03$$

$$T(23) = 1$$

$$K(20,f) = .00301$$

$$R_2 = F \times T \times K = 2.03 \times 1 \times .00301 = .00611$$

Exposure 3a:

$$F(3) = 3 + 3^2/116 = 3.08$$

$$T(23) = 1$$

$$K(21,f) = .00287$$

$$R_{3a} = F \times T \times K = 3.08 \times 1 \times .00287 = .00884$$

Exposure 3b:

$$F(6) = 6 + 6^2/116 = 6.31$$

$$T(23) = 1$$

$$K(21,f) = .00287$$

$$R_{3b} = F \times T \times K = 6.31 \times 1 \times .00287 = .0181$$

Exposures 4, 5, and 6:

$$F(1.1 + 0.6 + 0.7) = F(2.4) = 2.4 + 2.4^2/116 = 2.45$$

$$T(9) = .926$$

$$K(35,f) = .00142$$

$$R_{4,5,6} = F \times T \times K = 2.45 \times .926 \times .00142 = .00322$$

$$R = R_1 + R_2 + R_{3a} + R_{3b} + R_{4,5,6} = .00304$$

$$+ .00611 + .00884 + .0181 + .00322 = .0393$$

$$PC = R/(1+R) = .0393/1.0393 = .038 = 4\%.$$

The uncertainty surrounding PC estimates is discussed in Chapter VII, and Section VII-0 includes a derivation of approximate 90 percent credibility intervals for PC estimates.

To provide an orientation to the general magnitude of the PC values that result from the procedures described here, Fig X-11 has been drawn for tissue doses of 10 and 100 rad of low-LET radiation, and PC values plotted by age at exposure, for both males and females, and on the assumption that the minimal latent period has been satisfied. The vertical scale is logarithmic and curves are presented for only two radiation dose levels. For these and other reasons interpolation is to be discouraged.

Fig. X-11

KIDNEY AND BLADDER CANCER
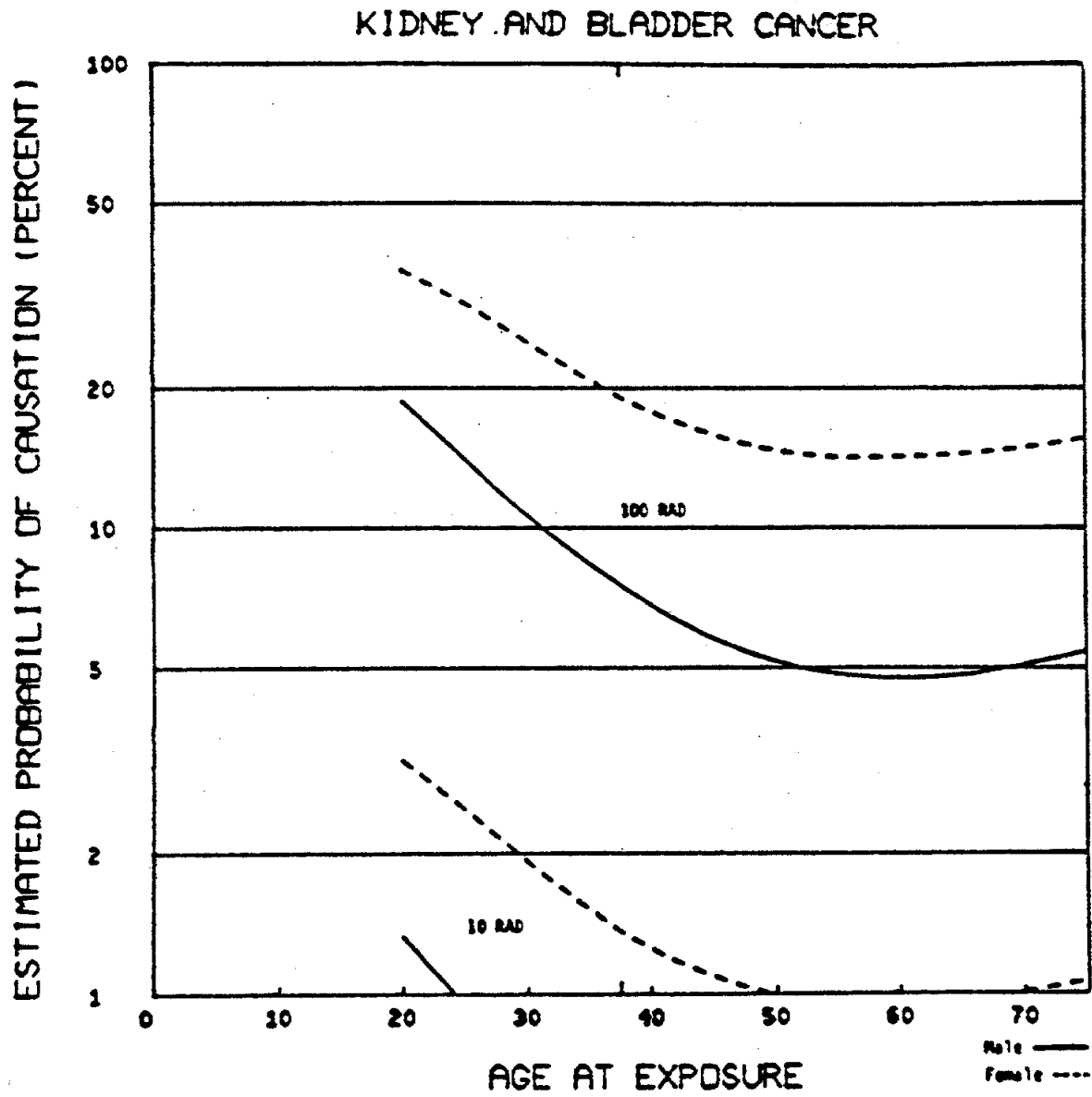
Table X-11. Kidney and Bladder Cancer: Relative Excess
K(A_1,S) by Exposure Age A_1 and Sex S

A_1	Sex		A_1	Sex	
	Male	Female		Male	Female
20	.00124	.00301	48	.000306	.000958
21	.00116	.00287	49	.000300	.000943
22	.00108	.00273	50	.000294	.000930
23	.00101	.00260	51	.000289	.000920
24	.000945	.00247	52	.000285	.000911
25	.000883	.00235	53	.000281	.000904
26	.000826	.00223	54	.000278	.000898
27	.000772	.00211	55	.000275	.000895
28	.000724	.00200	56	.000273	.000892
29	.000680	.00190	57	.000271	.000891
30	.000642	.00180	58	.000270	.000892
31	.000607	.00172	59	.000269	.000893
32	.000575	.00163	60	.000269	.000894
33	.000546	.00156	61	.000269	.000896
34	.000519	.00149	62	.000269	.000898
35	.000495	.00142	63	.000270	.000901
36	.000472	.00136	64	.000271	.000904
37	.000451	.00130	65	.000272	.000908
38	.000431	.00125	66	.000274	.000913
39	.000413	.00121	67	.000276	.000919
40	.000396	.00117	68	.000279	.000925
41	.000380	.00113	69	.000283	.000932
42	.000366	.00110	70	.000286	.000940
43	.000353	.00107	71	.000290	.000949
44	.000341	.00104	72	.000294	.000958
45	.000331	.00102	73	.000299	.000968
46	.000322	.000995	74	.000303	.000980
47	.000314	.000975	75	.000308	.000993

12. Thyroid Cancer (193 in ICDA-8)

The thyroid tables were constructed on the basis of the assumptions
and principles of Chapter V and the procedures described in Chapters VI
and IX. The risk coefficients used in making the tables, however, were
modified from the published BEIR III values and are given in Table VI-1.
The BEIR III coefficients were based largely on the exposure of children
and the data available in 1978-79, when the report was prepared, seemed
insufficient to support clinical impressions of age differentials in risk
(4). A central value of 4.0 excess cancers per million persons per year
per rad was postulated on the basis of the literature available at that
time, and the female/male ratio of risk, 2.6, was taken from preliminary
data (40 clinical cases) on the A-bomb survivors (87) to yield estimates
of 5.8 for females and 2.2 for males, regardless of age at exposure.

Data concerning the incidence of thyroid cancer are especially uncer-
tain because of difficulty of ascertainment. Thyroid cancers are usually
indolent; they are often slow growing and may not come to medical attention
unless they are sought by active investigation. Since active screening for
thyroid cancer will often be undertaken upon population groups in which
it is suspected that thyroid cancers may have been induced by radiation,
excesses may be found, not only because the incidence is increased but
because diligent investigation has identified cancers that would otherwise
not come to attention.

Since the BEIR III report was prepared, additional data have been
published on the Israeli tinea capitis series (88) and on the A-bomb
survivors (29,89). In addition, the Working Group has had access to a
near-final manuscript on 178 clinical cases among the A-bomb survivors
(90). The Israeli series is limited to persons who were children at the
time of exposure, but the recent reports on the A-bomb survivors contain
clear evidence of age variation in risk and also provide a more stable
estimate of the ratio of female to male risk coefficients, 3.5. The US
literature suggests an average risk coefficient of about 3.3 excess
cancers per million persons per year per rad for those exposed as children,
and the Working Group has employed this value, rather than 4.0, together
with the female/male ratio of 3.5, to obtain the final coefficients of
1.5 for males and 5.0 for females. Since the observed risks in A-bomb
survivors 20 or older at exposure are about one-third of those for survivors
exposed before age 20, this fraction was used to estimate approximate
coefficients for the older group, 0.5 for males and 1.5 for females.

Although there is some evidence favoring a minimum latent period of
5 years for thyroid cancer (91), it was decided to use the standard
assumption of 10 years (smoothed over the interval 5-10 years) made for
all solid tumors as described in Chapter V-C. Published dose-response
information on radiation-induced thyroid cancer is not extensive, but it
clearly suggests linearity (91). In addition, in the large unpublished
series of Ishimaru et al. the excess thyroid cancer incidence among
A-bomb survivors is best fitted by a linear function of dose (90).
.Despite its general preference for the linear-quadratic dose-response
function, therefore, the Working Group chose to base its PC estimation
procedures for thyroid cancer on linearity. The distribution of radiation-
induced cases over time was assumed to follow the relative risk model

although there is very little published thyroid cancer information with which to test this assumption.

The PC estimates calculated for thyroid cancer pertain to external X and gamma irradiation, not to the radioisotopes of iodine. Although iodine-131 is thought to be the major source of irradiation of thyroid tissues in individuals exposed to fallout from the weapons tests, the existing human data are not of sufficient cogency to provide a direct basis for quantitative estimates of riks; furthermore, there is contro-versy over the biological effectiveness of iodine-131 beta radiation relative to X rays and gamma rays. An Ad Hoc Working Group on Thyroid/Iodine Assessment, also mandated by the Orphan Drug Act (Public Law 97-414, Section 7a) is currently reviewing the available data and research needs in this area.

It is the SEER data on the incidence of thyroid cancer for all repor-ting areas combined except Puerto Rico, and all races combined, for the period 1973-1981, that is the source of the normal incidence rates employed here (8). For thyroid cancer known risk factors are neither numerous nor influential (92); there is, however, some variation in the SEER tables· for individual reporting areas (see Tables VII-1 and VII-2).

For thyroid cancer the relative excess, R, in the basic equation

$$PC = R/(1 + R)$$

is found as the product of three functions, i.e.,

$$R = F(D) \times T(Y) \times K(A_1,S)$$

where $F(D)$ represents the influence of the low-LET tissue dose (D), $T(Y)$ represents variation in R over time in years (Y) after exposure, and $K(A_1,S)$ represents the relative excess thyroid cancer per rad for a person of sex S and age at exposure A_1, when both F and T = 1.

Under the linear model assumed for thyroid cancer, F = D where D is the low-LET tissue dose in rad. For the thyroid the influence of time (T) on relative risk depends only on years from exposure to diagnosis (Y). The simple function T, the latency factor, is tabled below:

Y	0-4	5	6	7	8	9	10+
T	0	.074	.259	.500	.741	.926	1.

The standardized relative risk of excess thyroid cancer, K, is given in the accompanying Table X-12 for each sex and individual year of age (completed years) from birth to 75.

A few examples should make it clear how the PC values are to be obtained.

Example 1 A female, aged 10 when exposed to 5 rad of low-LET radiation to thyroid tissue, with diagnosis 9.9 years later, and assumed to be typical of her age and sex with respect to the normal risk of thyroid cancer. That is, D = 5, A_1 = 10, and Y = 9.

- 256 -

$$F(D) = 5$$

$$T(Y) = T(9) = .926$$

$$K(A_1,S) = K(10,f) = .0594$$

$$\text{then } R = F \times T \times K = 5 \times .926 \times .0594 = .275$$

$$\text{and } PC = R/(1 + R) = .275/1.275 = .216 \text{ or } 22\%.$$

Example 2   A female exposed twice to low-LET radiation to thyroid tissue, 5 rad at age 10 and 2 rad at age 15, with diagnosis of thyroid cancer at age 25, 9.8 years after the latter exposure. Again, it is assumed that she is representative of her age and sex with respect to the normal risk of thyroid cancer. We must combine two values of R, one for each exposure.

Exposure 1, at age 10, when $D = 5$, $A_1 = 10$, and $Y = 15$

$$F(D) = 5$$

$$T(15) = 1$$

$$K(10, f) = .0594$$

$$\text{then } R_1 = F \times T \times K = 5 \times 1 \times .0594 = .297$$

Exposure 2, at age 15, when $D = 2$, $A_1 = 15$, and $Y = 9$

$$F(D) = 2$$

$$T(9) = .926$$

$$K(15, f) = .0535$$

$$\text{then } R_2 = F \times T \times K = 2 \times .926 \times .0535 = .0991$$

$$\text{the total } R = R_1 + R_2 = .297 + .099 = .396$$

$$\text{and } PC = R/(1 + R) = .396/1.396 = .284, \text{ or } 28\%.$$

Example 3   A thyroid cancer was diagnosed at age 44 in a woman following several exposures to low-LET radiation at various ages. The first, of one rad to the thyroid, occurred at age 20, 24 years and 2 months before diagnosis ($Y = 24$). The second, to 2 rad, occurred 4 months later, at the same age ($A_1 = 20$) but 23 years and 10 months before diagnosis ($Y = 23$). At age 21, 23 years and 3 months before diagnosis, a 9-rad total dose was received over a 36-hour period at the continuous rate of 250 millirad per hour ($Y = 23$). Finally, at age 35, three exposures, to 1.1, 0.6, and 0.7 rad, respectively, were received on consecutive days, 9 years and 2 months prior to diagnosis ($Y = 9$). The first, second, and third exposures should be considered separately, because exposures 1 and 2 correspond to different values of Y, and exposures 2 and 3 to different exposure ages. The 9-rad continuous exposure delivered over 36 hours can be treated as a

single exposure because estimated risk under the linear model depends only upon the total dose. Similarly, the three exposures at age 35 can be treated as a single exposure.

Exposure 1:

$$F(D) = 1$$

$$T(Y) = T(24) = 1$$

$$K(20,f) = .0374$$

$$R_1 = F \times T \times K = 1 \times 1 \times .0374 = .0374$$

Exposure 2:

$$F(D) = 2$$

$$T(23) = 1$$

$$K(20,f) = .0374$$

$$R_2 = F \times T \times K = 2 \times 1 \times .0374 = .0748$$

Exposure 3:

$$F(D) = 9$$

$$T(23) = 1$$

$$K(21,f) = .0331$$

$$R_3 = F \times T \times K = 9 \times 1 \times .0331 = .2979$$

Exposures 4, 5, and 6:

$$F(1.1 + 0.6 + 0.7) = F(2.4) = 2.4$$

$$T(9) = .926$$

$$K(35,f) = .0175$$

$$R_{4,5,6} = F \times T \times K = 2.4 \times .926 \times .0175 = .0389$$

$$R = R_1 + R_2 + R_3 + R_{4,5,6} = .0374 + .0748$$
$$+ .2979 + .0389 = .449$$

$$PC = R/(1 + R) = .449/1.449 = .310 \text{ or } 31\%.$$

The uncertainty surrounding PC estimates is discussed in Chapter VII, and Section VII-0 includes a derivation of approximate 90 percent credibility intervals for PC estimates.

To provide an orientation to the general magnitude of the PC values that result from the procedures described here, Fig X-12 has been drawn for tissue doses of 1, 10, and 100 rad of low-LET radiation, and PC values plotted by age at exposure, for both males and females, and on the assumption that the minimal latent period has been satisfied. The vertical scale is logarithmic and curves are presented for only three radiation dose levels. For these and other reasons interpolation is to be discouraged.

Fig. X-12
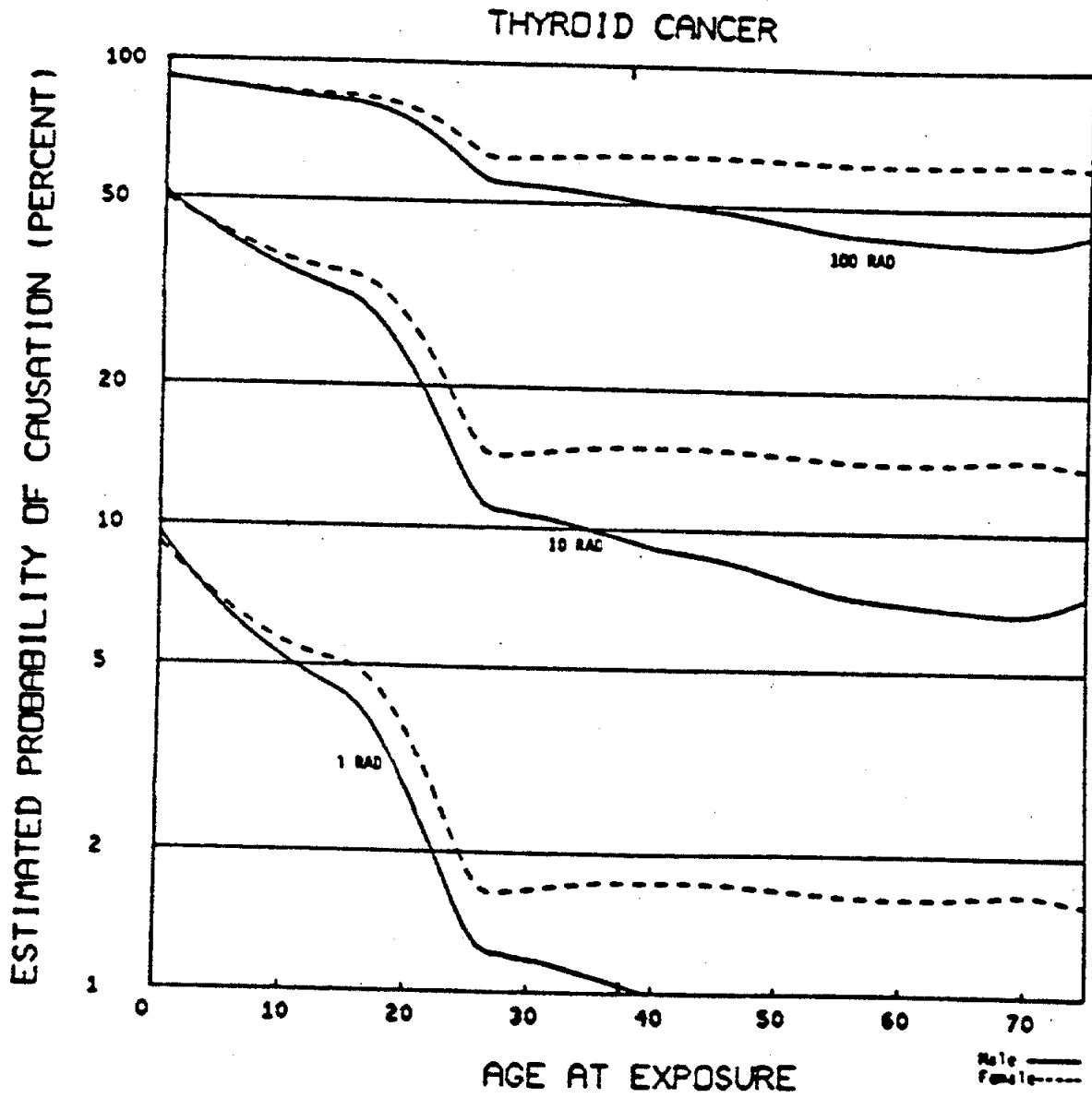
THYROID CANCER

Table X-12. Thyroid Cancer: Relative Excess $K(A_1,S)$
by Exposure Age A_1 and Sex S

A_1	Sex		A_1	Sex	
	Male	Female		Male	Female
0	.106	.100	38	.0104	.0176
1	.0965	.0931	39	.0102	.0176
2	.0885	.0871	40	.0101	.0176
3	.0819	.0820	41	.00992	.0176
4	.0762	.0775	42	.00981	.0176
5	.0713	.0735	43	.00971	.0176
6	.0671	.0700	44	.00961	.0176
7	.0634	.0668	45	.00949	.0175
8	.0601	.0640	46	.00935	.0175
9	.0573	.0615	47	.00919	.0174
10	.0547	.0594	48	.00902	.0173
11	.0525	.0577	49	.00884	.0172
12	.0505	.0563	50	.00866	.0171
13	.0487	.0552	51	.00848	.0170
14	.0471	.0543	52	.00831	.0169
15	.0455	.0535	53	.00814	.0168
16	.0430	.0517	54	.00799	.0167
17	.0397	.0490	55	.00786	.0166
18	.0359	.0456	56	.00776	.0165
19	.0320	.0416	57	.00769	.0165
20	.0282	.0374	58	.00763	.0164
21	.0246	.0331	59	.00758	.0164
22	.0213	.0289	60	.00752	.0164
23	.0184	.0250	61	.00747	.0164
24	.0158	.0215	62	.00741	.0164
25	.0139	.0188	63	.00736	.0164
26	.0127	.0171	64	.00731	.0164
27	.0123	.0166	65	.00726	.0165
28	.0122	.0167	66	.00722	.0166
29	.0120	.0168	67	.00718	.0166
30	.0119	.0169	68	.00714	.0167
31	.0118	.0170	69	.00712	.0168
32	.0116	.0172	70	.00713	.0169
33	.0114	.0173	71	.00719	.0168
34	.0112	.0174	72	.00729	.0167
35	.0110	.0175	73	.00745	.0164
36	.0108	.0176	74	.00764	.0162
37	.0106	.0176	75	.00784	.0160

13. Excluded Sites

Although it is generally accepted that ionizing radiation may increase the risk of virtually any form of cancer, for many sites compelling human data on its causative role are lacking, and for still others the existing data are inadequate for the present purpose. For example, the BEIR III report lists the following sites or tissues under the category of those in which radiation-induced cancer has not been observed: prostate, uterus and cervix, testis, mesentery and mesothelium, and chronic lymphocytic leukemia. Sites or tissues in which the magnitude of the dose-specific risk is uncertain are specified as: larynx, nasal sinuses, parathyroid, ovary, and connective tissues (4). In addition, the BEIR III committee presented estimates for lymphoma that no longer seem supportable; if, indeed, certain malignant lymphomas are radiogenic, the evidence remains too tenuous and inadequate to serve as the basis of PC calculations. Although excess mortality from malignant lymphoma has been reported in the British ankylosing spondylitis series (3), among the U.S. radiologists (93), and among the Japanese A-bomb survivors (94), most of the evidence has been based on death certificate diagnoses and on small numbers. No statistically significant excess is evident in the most recent report on mortality among the A-bomb survivors (28) or in the reports based on the tumor registries (29,30). In their 1972 review of the evidence Anderson et al. pointed to differences in the pathogenesis of leukemia and malignant lymphoma and concluded that radiation-induced malignant lymphoma can be observed only following very high-dose, possibly near-lethal, exposures (95).

Multiple myeloma is a special case, worthy of further discussion. Popularized as a radiogenic form of cancer by the first Hanford report (43), multiple myeloma continues to have uncertain status as a radiogenic tumor. Cuzik has summarized the data from 12 irradiated populations in which some association has been reported between multiple myeloma and exposure to ionizing radiation, but these provide no basis for quantitative risk estimates (96). Miller and Beebe have questioned Cuzik's pooling of dissimilar studies, some of which do not show a wave of leukemia before small excesses of multiple myeloma (97). Another perplexing factor was that, in no study, no matter how heavy the dose, was the excess of multiple myeloma more than marginal. A numerical basis for risk estimation can be derived from recent reports on mortality from multiple myeloma among A-bomb survivors (28,98) but histologically confirmed cases in the Nagasaki Tumor Registry (29) and the Hiroshima Tumor Registry (30) are considerably fewer and place the relationship in doubt.

Brain cancer has been reported in both of the tinea capitis series (20,88) but not in sufficient numbers of provide stable statistical estimates. Skin cancer is well-established as an effect of exposure to ionizing radiaton but not to low doses. No threshold dose has been agreed upon and there is no quantitative basis for risk estimates in the region of practical interest (4).

REFERENCES - Chapter X

1. Ichimaru, M., Ishimaru, T., Mikami, M., Yamada, Y., and Ohkita, T.,
   Incidence of Leukemia in a Fixed Cohort of Atomic Bomb Survivors and
   Controls, Hiroshima and Nagasaki, October 1950-December 1978. Technical
   Report 13-91, Hiroshima, Radiation Effects Research Foundation, 1981.

2. United Nations Scientific Committee on the Effects of Atomic Radiation,
   "Sources and Effects of Ionizing Radiation." Report to the General
   Assembly, Publ. E.77.1X.1. United Nations, New York, 1977.

3. Smith, P. G. and Doll, R., Mortality among Patients with Ankylosing
   Spondylitis after a Single Treatment Course with X-Ray. Br. Med. J.
   284: 449-460 (1982).

4. Committee on the Biological Effects of Ionizing Radiation, "The Effects
   on Populations of Exposure to Low Levels of Ionizing Radiation: 1980."
   National Academy Press, Washington, D.C., 1980.

5. Boice, J. D., Jr. and Day, M. E., Cancer Risk Following Radiotherapy of
   Cervical Cancer. In "Radiation Carcinogenesis: Epidemiolgy and
   Biological Significance" (J. D. Boice, Jr. and J. F. Fraumeni, Jr.,
   Eds.), pp. 161-179. Raven Press, New York, 1984.

6. Stewart, A. M. and Kneale, G. W., Prenatal Radiation Exposure and
   Childhood Cancer. Lancet 1: 42-43 (1971).

7. Monson, R. R., and MacMahon, B., Prenatal X-ray Exposure and Cancer
   in Children. In "Radiation Carcinogenesis: Epidemiology and Biological
   Significance" (J. D. Boice, Jr. and J. F. Fraumeni, Jr., Eds.), pp.
   97-105. Raven Press, New York, 1984.

8. Young, J. L., Jr., Percy, C. L., and Asire, A. J. (Eds.), "Surveillance,
   Epidemiology, and End Results: Incidence and Mortality Data, 1973-1977."
   National Cancer Institute Monograph 57. NIH Publication No. 81-2330.
   U.S. Government Printing Office, Washington, D.C., 1981.

9. Heath, C. W., Jr., The Leukemias. In "Cancer Epidemiology and Preven-
   tion" (D. Schottenfeld and J. F. Fraumeni, Jr., Eds.), pp. 728-738.
   W. Saunders, Philadelphia, 1982.

10. Rowland, R. E., Stehney, A. F., and Lucas, H. F., Jr., Dose-Response
    Relationships for Female Radium Dial Workers. Radiat. Res. 76: 368-
    383 (1978).

11. Mays, C. W., Spiess, H., and Gerspach, A., Skeletal Effects Following
    224-Ra Injections into Humans. Health Phys. 35: 83-90 (1978).

12. Mays, C. W. and Spiess, H., Epidemiological Studies of German Patients
    Injected with ^{224}Ra. In "Epidemiology Applied to Health Physics"
    (Proceedings of the Sixteenth Midyear Topical Meeting, Health Physics
    Society, Albuquerque NM, January 9-13, 1983), pp. 159-166, National
    Technical Information Service CONF-830101, Washington, D.C., 1983.

13. Land, C. E., Personal communication.

14. Fraumeni, J. F., Jr. and Boice, J. D. Jr.: Bone. In "Cancer Epidemiology and Prevention" (D. Schottenfeld and J. F. Fraumeni, Jr., Eds.), pp. 814-826, W. B. Saunders, Philadelphia, 1982.

15. Mulvihill, J. J., Miller, R. W., and Fraumeni, J. F., Jr., Genetics of Human Cancer. Raven Press, New York, 1977.

16. Saenger, E. L., Silverman, F. N., Sterling, T. D., and Turner, M. E., Neoplasia Following Therapeutic Irradiation for Benign Conditions in Childhood. Radiology 74: 889-904 (1960).

17. Janower, M. L. and Miettinen, O. S., Neoplasms after Childhood Irradiation of the Thymus Gland. J. Am. Med. Assoc. 215: 753-756 (1971).

18. Modan, B., Baidatz, D., Mart, H., Steinitz, R., and Levin, S. G., Radiation-Induced Head and Neck Tumours. Lancet 1: 277-279 (1974).

19. Hempelmann, L. H., Hall, W. J., Phillips, M., Cooper, R. A., and Ames, W. R., Neoplasms in Persons Treated with X-rays in Infancy: Fourth Survey in 20 Years. J. Natl. Cancer Inst. 55: 519-530 (1975).

20. Shore, R. E., Albert, R. E., and Pasternack, B. S., Follow-up Study of Patients Treated by X-ray Epilation for Tinea Capitis: Resurvey of Post-treatment Illness and Mortality Experience. Arch. Environ. Health 31: 21-28 (1976).

21. Schneider, A. B., Vavus, M. J., Stachura, M. E., Arnold, M. J., and Frohman, L. A., Salivary Gland Neoplasms as a Late Consequence of Head and Neck Irradiation. Ann. Intern. Med. 87: 160-164 (1978).

22. Maxon, H. R., Saenger, E. L., Buncher, C. R., Kereiakes, J. G., Thomas, S. R., Shafer, M. L., and McLaughlin, C. A., Radiation-associated Carcinoma of the Salivary Glands. A Controlled Study. Ann. Otol. Rhinol. Laryngol. 90: 107-108 (1981).

23. Land, C. E., Carcinogenic Effects of Radiation on the Human Digestive Tract and Other Organs. In "Radiation Carcinogenesis" (A. C. Upton, R. E. Albert, F. J. Burns, and R. E. Shore, Eds.), 1985, Elsevier North-Holland, New York, in press.

24. Belsky, J. L., Takeichi, N., Yamamoto, T., Cihak, R. W., Hirose, F., Ezaki, H., Inoue, S., and Blot, W. J., Salivary Gland Neoplasms Following Atomic Radiation: Additional Cases and Reanalysis of Combined Data in the Fixed Population, 1957-1970. Cancer 35: 555-559 (1975).

25. Takeichi, N., Horise, F., and Yamomoto, H., Salivary Gland Tumors in Atomic Bomb Survivors, Hiroshima, Japan. I. Epidemiologic Observations. Cancer 38: 2462-2468 (1976).

26. Court-Brown W. M., and Doll, R., Mortality from Cancer and Other Causes after Radiotherapy for Ankylosing Spondylitis. Br. Med. J. 2: 1327-1332 (1965).

27. Beebe, G. W., Kato, H., and Land, C. E., Studies of the Mortality of A-bomb Survivors. 6. Mortality and Radiation Dose, 1950-1974. Radiat. Res. 75: 138-201 (1978).

28. Kato, H., and Schull, W. J., Studies of the Mortality of A-bomb Survivors. 7. Mortality, 1950-1978. Part I. Cancer Mortality. Radiat. Res. 90: 395-432 (1982).

29. Wakabayashi, T., Kato, H., Ikeda, T., and Schull, W. T., Studies of the Mortality of A-bomb Survivors. 7. Mortality, 1950-1978. Part III. Incidence of Cancer in 1959-1978, Based on the Tumor Registry, Nagasaki. Radiat. Res. 93: 112-146 (1983).

30. Kato, H., et al., In preparation.

31. Day, N. E., and Munoz, N., Esophagus. In "Cancer Epidemiology and Prevention" (D. Schottenfeld and J. F. Fraumeni, Jr., Eds.), pp. 596-623. W. B. Saunders, Philadelphia, 1982.

32. Tuyns, A. J., Pequignot, G., and Jensen, O. M., Les Cancers de l'Oesophage en Ille-et-Villaine en Fonction des Niveaux de Consommation d'Alcool et de Tabac. Des Risques Qui Se Multiplient. Bull. Cancer (Paris) 64: 45-60 (1977).

33. Land, C. E., and Tokunaga, M., Induction Period. In "Radiation Carcinogenesis: Epidemiology and Biological Significance" (J. D. Boice, and J. F. Fraumeni, Jr., Eds.), pp. 421-436. Raven Press, New York, 1984.

34. Nomura, A., Stomach. In "Cancer Epidemiology and Prevention". (D. Schottenfeld and J. F. Fraumeni, Jr., Eds.), pp. 624-637. W. B. Saunders, Philadelphia, 1982.

35. Brinkley, D., and Haybittle, J. L., The Late Effects of Artificial Menopause by X-radiation. Br. J. Radiol. 42: 519-521 (1969).

36. Smith, P. G., and Doll, R., Late Effects of X-irradiation in Patients Treated for Metropathia Haemorrhagica. Br. J. Radiol. 49: 224-232 (1976).

37. Dickson, R. J., The Late Results of Radium Treatment for Benign Uterine Haemorrhage. Br. J. Radiol. 42: 582-594 (1969).

38. Wagoner, J. K., Leukemia and Other Malignancies Following Radiation Therapy for Gynecological Disorders. In "Radiation Carcinogenesis: Epidemiology and Biological Significance" (J. D. Boice, Jr. and J. F. Fraumeni, Jr., Eds.), pp. 153-160. Raven Press, New York, 1984.

39. Schottenfeld, D. and Winawer, S. J.: Large Intestine. In "Cancer Epidemiology and Prevention" (D. Schottenfeld and J. F. Fraumeni, Jr. Eds.), pp. 703-727. W. B. Saunders, Philadelphia, 1982.

40. Mays, C. W., Ed., Biological Effects of ^{224}Ra and Thorotrast. Proceedings of an International Symposium. Health Phys. 35: 1-174, (1978).

41. Falk, H., Liver. In "Cancer Epidemiology and Prevention" (D. Schottenfeld and J. F. Fraumeni, Jr. Eds.), pp. 668-682. W. B. Saunders, Philadelphia, 1982.

42. Steer, A., Moriyama, I. M., and Shimizu, K., ABCC-JNIH Pathology Studies. Hiroshima and Nagasaki. Report 3. The Autopsy Program and the Life Span Study, January 1951 - December 1970. Technical Report 16-73. Atomic Bomb Casualty Commission, Hiroshima, 1973.

43. Mancuso, T. F., Stewart, A., and Kneale, G., Radiation Exposures of Hanford Workers Dying from Cancer and Other Causes. Health Phys. 33: 369-385 (1977).

44. Hutchinson, G. B., MacMahon, B., Jablon, S., and Land, C. E., Review of Report by Mancuso, Stewart, and Kneale of Radiation Exposure of Hanford Workers. Health Phys. 37: 207-220 (1979).

45. Gilbert, E. S., and Marks, S., An Analysis of the Mortality of Workers in a Nuclear Facility. Radiat. Res. 79: 122-148 (1979).

46. Gilbert, E. S., and Marks, S., An Updated Analysis of Mortality of Workers in a Nuclear Facility. Radiat. Res. 83: 740-741 (1980).

47. Mack, T. M., Pancreas. In "Cancer Epidemiology and Prevention", (D. Schottenfeld, and J. F. Fraumeni, Jr., Eds.), pp. 639-667. W. B. Saunders, Philadelphia, 1982.

48. Sevc, J., Kunz, E., and Placek, V., Lung Cancer in Uranium Miners and Long-term Exposure to Radon Daughter Products. Health Phys. 30: 433-437 (1976).

49. Archer, V. E., Gilliam, J. D., and Wagoner, J. K., Respiratory Disease Mortality Among Uranium Miners. Ann. NY Acad. Sci. 271: 280-293 (1976).

50. DeVilliers A. J. and Wigle, D. T., Unpublished manuscript concerning Newfoundland fluorspar miners. Cited in reference 4: "Effects on Populations of Exposure to Low Levels of Ionizing Radiation: 1980", pp. 322-323, National Academy Press, Washington, D.C., 1980.

51. Blot, W. J., Akiba, S., and Kato, H., Ionizing Radiation and Lung Cancer: A Review Including Preliminary Results from a Case-Control Study among A-Bomb Survivors. In: "Atomic Bomb Survival Data: Utilization and Analysis" (R. L. Prentice, R. L. and D. J. Thompson, Eds.), pp. 235-248. SIAM (Society for Industrial and Applied Mathematics), Philadelphia, 1984.

52. Axelson, O. and Sundell, L., Mining, Lung Cancer and Smoking, Scand. J. Work Environ. Health 4: 46-52 (1978).

53. Edling, C., Lung Cancer and Smoking in a Group of Iron Ore Miners, Am. J. Ind. Med. 3: 191-199 (1982).

54. Radford, E. P. and St. Clair Renard, K. G., Lung Cancer in Swedish Iron Miners Exposed to Low Doses of Radon Daughters. N. Engl. J. Med. 310: 1485-1494 (1984).

55. Thomas, D. C. and McNeill, K. G., "Risk Estimates for the Health Effects of Alpha Radiation" (INFO-0081). Atomic Energy Control Board, Ottawa, Canada K1P 5S9, 1982.

56. Archer, V. E., Wagoner, J. K. and Lundin, F. E., Uranium Mining and Cigarette Smoking: Effects on Man. J. Occup. Med. 15: 204-211 (1973).

57. Damber, L. and Larsson, L. G., Combined Effects of Mining and Smoking in the Causation of Lung Carcinoma, Acta Radiol. Oncol. 21: 305-313 (1982).

58. Larsson, L. G. and Damber, L., Interaction between Underground Mining and Smoking in the Causation of Lung Cancer: A Study of Non-Uranium Miners in Northern Sweden, Cancer Detect. Prev. 5: 385-389 (1982).

59. Whittemore, A. S. and McMillan, A., Lung Cancer Mortality Among U.S. Uranium Miners: A Reappraisal, J. Natl. Cancer Inst. 71: 489-499 (1983).

60. Jacobi, W., Paretzke, H. G., and Schindel, F., Lung Cancer Risk Assessment of Radon-Exposed Miners on the Basis of a Proportional Hazards Model. In "Proceedings of the International Conference on Occupational Radiation Safety in Mining", Oct. 14-18, 1984, Toronto, Canada, in press.

61. Lundin, F. E., Jr., Wagoner, J. K., and Archer, V. E., "Radon Daughter Exposure and Respiratory Cancer: Quantitative and Temporal Aspects." National Institute for Occupational Safety and Health, National Institute of Environmental Health Sciences Joint Monograph No. 1, National Technical Information Service, Springfield, VA, 1971.

62. NCRP Report No. 78, "Evaluation of Occupational and Environmental Exposures to Radon and Radon Daughters in the United States." National Council on Radiation Protection and Measurements, Washington, D.C., 1984.

63. Harley, N. H. and Pasternack, B. S., A Model for Predicting Lung Cancer Risks Induced by Environmental Levels of Radon Daughters, Health Phys. 40: 307-316 (1981).

64. Jacobi, W., The New ICRP Recommendations on Occupational Limits for Radon Daughters. In: "Radiation Hazards in Mining" (M. Gomez, Ed.), pp. 503-510. Society of Mining Engineers of the American Institute of Mining, Metallurgical and Petroleum Engineers, Inc., New York, 1981.

65. ICRP Publication 32, "Limits for Inhalation of Radon Daughters by Workers." International Commission on Radiation Protection, Pergamon Press, Oxford-New York, 1981.

66. Ellett, W. E. and Nelson, N., Epidemiology and Risk Assessment. In: "Proceedings of the Seventh ORNL Life Sciences Symposium: Indoor Air and Human Health", Knoxville, TN, Oct. 29-31, 1981. Oak Ridge Associated Universities, Oak Ridge, TN, in press.

67. Darby, S. C., Nakashima, E., and Kato, H., "Parallel Analysis of Cancer Mortality among Atomic Bomb Survivors and Patients with Ankylosing Spondylitis Given X-ray Therapy." RERF Technical Report, Radiation Effects Research Foundation, Hiroshima, Japan, in press.

68. Steer, A., Land, C. E., Moriyama, I. M., Yamamoto, T., Asano, M., and Sanefuji, H., Accuracy of Diagnosis of Cancer Among Autopsy Cases: JNIH-ABCC Population for Hiroshima and Nagasaki. Gann 67: 623-632 (1976).

69. Fraumeni, J. F., Jr. and Blot, W. J., Lung and Pleura. In "Cancer Epidemiology and Prevention" (D. Schottenfeld and J. F. Fraumeni, Jr., Eds.), pp. 564-582. W. B. Saunders, Philadelphia, 1982.

70. Tokunaga, M., Norman, J. E., Jr., Asano, M., Tokuoka, S., Ezaki, H., Nishimori, I., and Tsuji, Y., Malignant Breast Tumors Among Atomic Bomb Survivors. Hiroshima and Nagasaki, 1950-1974. J. Natl. Cancer Inst. 62: 1347-1359 (1979). [RERF TR 17-77].

71. Boice, J. D., Jr. and Monson, R. R., Breast Cancer in Women after Repeated Fluoroscopic Examinations of the Chest. J. Natl. Cancer Inst. 59: 823-832 (1977).

72. Shore, R. E., Hemplemann, L. H., Kowaluk, E., Mansur, P. S., Pasternack, B. S., Albert, R. E., and Haughie, G. E., Breast Neoplasms in Women Treated with X-rays for Acute Postpartum Mastitis. J. Natl. Cancer Inst. 59: 813-822 (1977).

73. Boice J. D., Jr., Land, C. E., Shore, R. E., Norman, J. E., and Tokunaga, M., Risk of Breast Cancer Following Low-Dose Exposure. Radiology 131: 284-296 (1979).

74. Land, C. E., Boice, J. D., Jr., Shore, R. E., Norman, J. E., and Tokunaga, M., Breast Cancer Risk from Low-dose Exposures to Ionizing Radiation: Results of Parallel Analysis of Three Exposed Populations of Women. J. Natl. Cancer Inst. 65: 353-376 (1980).

75. Waterhouse, J., Muir, C., Shanmugaratham, K., and Powell, J., Eds., "Cancer Incidence in Five Continents", Vol IV. International Agency for Research on Cancer, Lyon, 1982.

76. Baral, E., Larsson, L., and Mattsson, B., Breast Cancer Following Irradiation of the Breast. Cancer 40: 2905-2910 (1977).

77. Tokunaga, M., Land, C. E., Yamamoto, T., Asano, M., Tokuoka, S., Ezaki, H., and Nishimori, I., Breast Cancer in Japanese A-bomb Survivors. Lancet 2: 924 (1982).

78. Tokunaga, M., Land, C. E., Yamamoto, T., Asano, M., Tokuoka, S., Ezaki, H., and Nishimori, I., Breast Cancer Among Atomic Bomb Survivors. In "Radiation Carcinogenesis: Epidemiology and Biological Significance" (J. D. Boice, Jr. and J. F. Fraumeni, Jr., Eds.), pp. 45-56. Raven Press, New York, 1984.

79. Hildreth, N. G., Shore, R. E., and Hempelmann, L. H., Risk of Breast Cancer among Women Receiving Radiation Treatment in Infancy for Thymic Enlargement. Lancet 2: 273 (1983).

80. Howe, G. R., The Epidemiology of Radiogenic Breast Cancer. In "Radiation Carcinogenesis: Epidemiology and Biological Significance" (J. D. Boice, Jr. and J. F. Fraumeni, Jr., Eds.), pp. 119-129. Raven Press, New York, 1984.

81. NCRP Report No. 64, "Influence of Dose and Its Distribution in Time on Dose-Response Relationships for Low-LET Radiation." National Council on Radiation Protection and Measurements, Washington, D.C., 1980.

82. Mackenzie, I., Breast Cancer Following Multiple Fluoroscopies. Br. J. Cancer 19: 1-8 (1965).

83. Advisory Committee on the Biological Effects of Ionizing Radiation, "The Effects on Populations of Exposure to Low Levels of Ionizing Radiation." National Academy of Sciences, Washington, D.C., 1972.

84. Petrakis, N. L., Ernster, V. L., and King, M.-C., Breast. In "Cancer Epidemiology and Prevention" (D. Schottenfeld and J. F. Fraumeni, Jr., Eds.), pp. 855-870. W. B. Saunders, Philadelphia, 1982.

85. Morrison, A. S., and Cole, P., Urinary Tract. In "Cancer Epidemiology and Prevention" (D. Schottenfeld and J. F. Fraumeni, Jr., Eds.), pp. 925-937. W. B. Saunders, Philadelphia, 1982.

86. Cole, P., et al, Occupation and Cancer of the Lower Urinary Tract. Cancer 29: 1250-1260 (1972).

87. Parker, L. N., Belsky, J. L., Yamamoto, T., Kawamoto, S., and Keehn, R. J., Thyroid Carcinoma after Exposure to Atomic Radiation. A Continuing Survey of a Fixed Population, Hiroshima and Nagasaki, 1958-1971. Technical Report 5-73. Radiation Effects Research Foundation, Hiroshima, 1973.

88. Ron, E., and Modan, B., Thyroid and Other Neoplasms Following Childhood Scalp Irradiation. In "Radiation Carcinogenesis: Epidemiology and Biological Significance" (J. D. Boice, Jr. and J. F. Fraumeni, Jr., Eds.), pp. 139-151. Raven Press, New York, 1984.

89. Prentice, R. L., Kato, H., Yoshimoto, K., and Mason, M., Radiation Exposures and Thyroid Cancer Incidence Among Hiroshima and Nagasaki Residents. In "Third Symposium on Epidemiology and Cancer Registries

in the Pacific Basin", National Cancer Institute Monograph 62, pp. 207-212. Government Printing Office, Washington, D.C., 1982.

90. Ishimaru, T., et al., Incidence of Thyroid Cancer among Atomic Bomb Survivors and Controls, Hiroshima and Nagaskai, 1958-1979: Relationship to Radiation Dose Absorbed by Thyroid Gland. Unpublished manuscript dated September 20, 1983.

91. Shore, R. E., Radiation-Induced Thyroid Cancer. In "Radiation Carcinogenesis: Epidemiology and Biological Significance" (J. D. Boice, Jr., and J. F. Fraumeni, Jr., Eds.), pp. 131-138. Raven Press, New York, 1984.

92. Ron, E. and Modan, B., Thyroid. In "Cancer Epidemiology and Prevention" (D. Schottenfeld and J. F. Fraumeni, Jr. Eds.), pp. 837-854. W. B. Saunders, Philadelphia, 1982.

93. Matanoski, G. M., Seltser, R., Sartwell, P. E., Diamond, E. L., and Elliott, E. A., The Current Mortality Rates of Radiologists and Other Physician Specialists: Specific Causes of Death. Am. J. Epidemiol. 101: 199-210, (1975).

94. Anderson, R. E., and Ishida, K., Malignant Lymphoma in Atomic Bomb Survivors, Hiroshima. Ann. Intern. Med. 61: 853-862 (1964).

95. Anderson, R. E., Nishiyama, H., Ii, Y., Ishida, K., and Okabe, N., Pathogenesis of Radiation-Related Leukemia and Lymphoma. Lancet 1: 1060-1062 (1972).

96. Cuzik, J., Radiation-induced Myelomatosis. N. Engl. J. Med. 304: 204-210, (1981).

97. Miller, R. W., and Beebe, G. W., Leukemia, Lymphoma, and Multiple Myeloma. In "Radiation Carcinogenesis" (A. C. Upton, R. E. Albert, F. J. Burns, and R. E. Shore, Eds.). Elsevier North-Holland, New York, in press.

98. Ichimaru, M., Ishimaru, T., Mikami, M., and Matsunaga, M., Multiple Myeloma among Atomic Bomb Survivors, 1950-1976: Relationship to Radiation Dose Absorbed by Marrow. J. Natl. Cancer Inst. 69: 323-328 (1982).

APPENDIX I

ILLUSTRATIVE PC TABLES

The complexity of the algorithms of the PC calculation is such that
systematic tables of the extent called for in the Orphan Drug Act would
prove unwieldy in practice and might invite more error than the alternative
procedure of ad hoc calculation based on a few reference tables for each
site. In adopting the latter route in its presentation, the Working Group
nevertheless was persuaded that some illustrative PC tables would usefully
supplement the graphic summaries of Chapter X.

PC tables have been prepared for tissue doses of 1, 10 and 100 rad,
and, for lung cancer (Table PC-9-1), for increments of cumulative exposure,
in WLM, to inhaled radon and radon daughter products. For the latter table
only, alternative PC values are presented, reflecting various choices of
risk coefficients as discussed in Chapter X-9. All other tables, with the
exception of the tables for bone cancer associated with exposure to alpha
particle radiation from radium-224, pertain only to low-LET radiation and
may not be used for exposure to high-LET radiation. Except for leukemia
and bone cancer, the tabulated coefficients from which the PC values are
calculated do not depend upon age at diagnosis. With the same exceptions,
dependence on time after exposure is restricted to multiplication of the
relative excess risk by a factor $T(Y)$ which increases from zero during
years $Y = 0-4$ to one for $Y \geq 10$. Thus it is sufficient to tabulate PC
values by radiation dose, sex, and age at exposure, for $Y \geq 10$. For
leukemia and bone cancer, on the other hand, the PC depends upon age at
diagnosis as well, and in the interests of brevity, separate tables of
PC, tabulated by sex, dose, and age at diagnosis, are presented only for
exposure ages 0 to 70 in steps of 10.

Interpolation on exposure age is not recommended for leukemia or
bone cancer because of the added complexity of dependence upon age at
diagnosis, and is unnecessary for other cancer sites. Interpolation on
dose is impracticable, except for interpolation on WLM in Table PC-9-I,
because PC values are given for only three dose values. It is, in any
case, easy to calculate PC values from the relevant tables in Chapter X.

A simple mathematical relationship holds between the PC values
corresponding to any two dose values, for any site, provided that all
other factors, like age at exposure, time from exposure to cancer diagnosis,
and sex, are the same. Let PC_1 denote the tabulated PC value for dose
D_1, and let PC_2 denote the (untabulated) value for dose D_2. Then

$$\frac{1}{PC_2} = 1 + \frac{1-PC_1}{PC_1} \frac{F(D_1)}{F(D_2)}$$

where $F(D) = D$ for breast or thyroid cancer following exposure to low-LET
radiation or for bone cancer following exposure to radium-224, and $F(D) =
D + D^2/116$ for other cancers following exposure to low-LET radiation. The
above relationship is not recommended for routine use because the tabulated
PC values are given to a lower degree of precision than the risk coefficients
in Chapter X.

- 271 -

The tables appearing below are:

PC-1-A   Chronic granulocytic leukemia

PC-1-B   Acute leukemia

PC-1-C   All leukemia except CLL

PC-2   Bone cancer following exposure to radium-224

PC-3   Salivary gland cancer

PC-4   Esophageal cancer

PC-5   Stomach cancer

PC-6   Colon cancer

PC-7   Liver cancer

PC-8   Pancreatic cancer

PC-9   Lung cancer

PC-10   Cancer of the female breast

PC-11   Kidney or bladder cancer

PC-12   Thyroid cancer.

Table PC-1-A-0. Chronic Granulocytic Leukemia Following
   Exposure at Age 0, by Age A_2 at Diagnosis, Sex, and Dose
   in Rad of Low-LET Radiation. PC in Percent, to Two
   Significant Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
2	29.	82.	99.	34.	85.	99.
3	52.	92.	99.	56.	93.	99.
4	56.	93.	99.	56.	93.	99.
5	57.	93.	99.	52.	92.	99.
6	56.	93.	99.	47.	91.	99.
7	55.	93.	99.	43.	89.	99.
8	53.	92.	99.	41.	88.	99.
9	51.	92.	99.	40.	88.	99.
10	49.	91.	99.	39.	87.	99.
11	47.	91.	99.	37.	86.	99.
12	46.	90.	99.	35.	85.	99.
13	42.	89.	99.	30.	83.	99.
14	37.	86.	99.	26.	79.	98.
15	31.	83.	99.	21.	74.	98.
16	27.	80.	99.	18.	70.	98.
17	23.	76.	98.	16.	67.	97.
18	19.	72.	98.	15.	65.	97.
19	16.	68.	97.	15.	65.	97.
20	14.	63.	97.	15.	65.	97.
21	11.	58.	96.	14.	64.	97.
22	9.7	54.	95.	12.	59.	96.
23	7.8	48.	94.	9.7	54.	95.
24	6.0	41.	92.	8.0	48.	94.
25	4.8	35.	90.	6.7	44.	93.
26	3.9	31.	88.	5.7	39.	92.
27	3.5	28.	87.	4.9	36.	90.
28	3.2	27.	86.	4.2	32.	89.
29	3.2	26.	86.	3.7	29.	88.
30	3.2	25.	86.	3.3	27.	86.
31	3.2	26.	86.	2.9	24.	85.
32	3.0	25.	85.	2.6	22.	83.
33	2.8	23.	84.	2.3	20.	81.
34	2.5	22.	83.	2.1	19.	80.
35	2.3	20.	81.	1.9	17.	78.

Table PC-1-A-10.   Chronic Granulocytic Leukemia Following
    Exposure at Age 10, by Age A_2 at Diagnosis, Sex, and Dose
    in Rad of Low-LET Radiation.[2] PC in Percent, to Two
    Significant Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
12	16.	67.	97.	11.	57.	96.
13	32.	84.	99.	22.	76.	98.
14	33.	84.	99.	23.	76.	98.
15	30.	82.	99.	20.	73.	98.
16	26.	79.	98.	17.	70.	98.
17	22.	75.	98.	15.	66.	97.
18	19.	71.	98.	14.	64.	97.
19	16.	67.	97.	14.	64.	97.
20	13.	62.	96.	14.	64.	97.
21	11.	57.	96.	13.	62.	97.
22	9.0	51.	95.	11.	58.	96.
23	7.1	45.	93.	8.9	51.	95.
24	5.4	38.	91.	7.2	46.	93.
25	4.2	32.	89.	6.0	41.	92.
26	3.4	28.	87.	5.0	36.	91.
27	3.0	25.	85.	4.2	32.	89.
28	2.8	23.	84.	3.6	29.	87.
29	2.7	23.	84.	3.1	26.	86.
30	2.7	23.	83.	2.7	23.	84.
31	2.6	22.	83.	2.4	21.	82.
32	2.5	21.	82.	2.1	19.	80.
33	2.2	20.	81.	1.9	17.	78.
34	2.0	18.	79.	1.7	15.	76.
35	1.8	16.	77.	1.5	14.	74.
36	1.6	15.	75.	1.3	13.	71.
37	1.5	14.	74.	1.2	12.	69.
38	1.4	13.	72.	1.1	11.	67.
39	1.3	12.	71.	.98	9.7	65.
40	1.2	12.	69.	.89	8.9	62.
41	1.1	11.	68.	.82	8.1	60.
42	1.1	10.	66.	.75	7.5	58.
43	.99	9.7	65.	.70	7.1	57.
44	.93	9.2	63.	.70	7.1	57.
45	.87	8.6	62.	.70	7.1	57.

Table PC-1-A-20. Chronic Granulocytic Leukemia Following
Exposure at Age 20, by Age A_2 at Diagnosis, Sex, and Dose
in Rad of Low-LET Radiation. PC in Percent, to Two
Significant Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
22	3.5	28.	87.	4.4	33.	89.
23	7.3	46.	94.	9.1	52.	95.
24	7.1	45.	93.	9.3	53.	95.
25	6.0	41.	92.	8.4	50.	94.
26	5.1	37.	91.	7.3	46.	94.
27	4.5	34.	90.	6.3	42.	93.
28	4.2	32.	89.	5.4	38.	91.
29	4.0	31.	89.	4.6	34.	90.
30	3.9	31.	88.	4.0	31.	88.
31	3.8	30.	88.	3.5	28.	87.
32	3.5	28.	87.	3.0	25.	85.
33	3.1	26.	86.	2.6	23.	83.
34	2.8	24.	84.	2.3	20.	81.
35	2.5	21.	82.	2.0	18.	79.
36	2.2	20.	81.	1.8	17.	77.
37	2.0	18.	79.	1.6	15.	75.
38	1.8	17.	78.	1.4	14.	73.
39	1.7	16.	76.	1.3	12.	71.
40	1.6	15.	75.	1.2	11.	68.
41	1.4	14.	73.	1.0	10.	66.
42	1.3	13.	71.	.94	9.3	64.
43	1.2	12.	70.	.88	8.7	62.
44	1.2	11.	68.	.87	8.6	62.
45	1.1	10.	67.	.86	8.6	62.
46	1.0	9.8	65.	.85	8.4	61.
47	.93	9.2	63.	.79	7.9	60.
48	.84	8.4	61.	.69	6.9	56.
49	.73	7.4	58.	.58	5.9	52.
50	.63	6.3	54.	.48	5.0	47.
51	.53	5.5	50.	.41	4.3	43.
52	.46	4.7	46.	.37	3.8	41.
53	.39	4.1	42.	.34	3.5	38.
54	.34	3.6	39.	.31	3.2	36.
55	.30	3.1	36.	.29	3.0	35.

Table PC-1-A-30. Chronic Granulocytic Leukemia Following Exposure at Age 30, by Age A_2 at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose			Dose		
	1	10	100	1	10	100
32	1.9	17.	78.	1.6	15.	75.
33	4.6	34.	90.	3.9	30.	88.
34	5.2	37.	91.	4.4	33.	89.
35	5.1	37.	91.	4.2	32.	89.
36	4.7	35.	90.	3.9	30.	88.
37	4.4	33.	89.	3.5	28.	87.
38	4.0	31.	89.	3.1	26.	86.
39	3.7	29.	88.	2.8	24.	84.
40	3.3	27.	86.	2.5	22.	82.
41	3.1	25.	85.	2.2	20.	81.
42	2.8	24.	84.	2.0	18.	79.
43	2.6	22.	83.	1.8	17.	77.
44	2.3	21.	82.	1.8	16.	77.
45	2.1	19.	80.	1.7	16.	77.
46	2.0	18.	79.	1.7	16.	76.
47	1.8	17.	77.	1.5	14.	74.
48	1.6	15.	75.	1.3	13.	71.
49	1.4	13.	72.	1.1	11.	67.
50	1.2	11.	69.	.91	9.0	63.
51	.99	9.7	65.	.77	7.8	59.
52	.84	8.4	61.	.68	6.9	56.
53	.72	7.2	57.	.61	6.2	53.
54	.62	6.3	53.	.56	5.7	51.
55	.53	5.5	50.	.52	5.3	49.
56	.45	4.8	46.	.47	4.8	47.
57	.40	4.2	43.	.43	4.4	44.
58	.35	3.6	39.	.39	4.0	42.
59	.31	3.2	36.	.35	3.6	39.
60	.27	2.8	33.	.31	3.2	36.
61	.24	2.5	31.	.28	2.9	34.
62	.21	2.2	28.	.25	2.6	32.
63	.19	2.0	26.	.22	2.3	29.
64	.18	1.9	24.	.20	2.1	27.
65	.16	1.7	23.	.17	1.8	24.

Table PC-1-A-40. Chronic Granulocytic Leukemia Following
    Exposure at Age 40, by Age A_2 at Diagnosis, Sex, and Dose
    in Rad of Low-LET Radiation. PC in Percent, to Two
    Significant Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
42	1.6	15.	75.	1.1	11.	68.
43	3.9	31.	88.	2.9	24.	84.
44	4.6	34.	90.	3.6	28.	87.
45	4.7	34.	90.	3.8	30.	88.
46	4.4	33.	90.	3.8	30.	88.
47	4.1	32.	89.	3.6	29.	87.
48	3.7	29.	88.	3.1	25.	85.
49	3.2	26.	86.	2.5	22.	83.
50	2.6	23.	83.	2.1	19.	80.
51	2.2	20.	81.	1.7	16.	77.
52	1.9	17.	78.	1.5	14.	74.
53	1.6	15.	75.	1.3	13.	72.
54	1.3	13.	71.	1.2	12.	69.
55	1.1	11.	68.	1.1	11.	67.
56	.96	9.5	64.	.99	9.7	65.
57	.83	8.2	61.	.89	8.8	62.
58	.71	7.2	57.	.79	7.9	60.
59	.61	6.2	53.	.70	7.1	57.
60	.53	5.5	50.	.62	6.3	54.
61	.47	4.8	46.	.55	5.6	51.
62	.41	4.3	43.	.49	5.0	48.
63	.37	3.8	41.	.43	4.5	44.
64	.33	3.5	38.	.38	3.9	41.
65	.30	3.2	36.	.33	3.4	38.
66	.27	2.9	34.	.29	3.1	35.
67	.25	2.6	32.	.26	2.7	32.
68	.22	2.4	29.	.24	2.5	31.
69	.20	2.1	27.	.24	2.5	30.
70	.18	1.9	25.	.23	2.4	30.
71	.16	1.7	22.	.22	2.3	29.
72	.14	1.5	20.	.20	2.1	27.
73	.12	1.3	18.	.17	1.8	24.
74	.10	1.1	16.	.14	1.5	21.
75	.090	.96	14.	.12	1.3	18.

Table PC-1-A-50. Chronic Granulocytic Leukemia Following Exposure at Age 50, by Age A_2 at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation.[2] PC in Percent, to Two Significant Digits or Three Decimal Places.

A_2	Male			Female		
	Dose					
	1	10	100	1	10	100
52	1.1	11.	67.	.91	9.0	63.
53	2.6	22.	83.	2.2	20.	81.
54	2.8	24.	84.	2.6	22.	83.
55	2.6	22.	83.	2.6	22.	83.
56	2.3	20.	81.	2.4	21.	82.
57	2.0	18.	79.	2.2	20.	81.
58	1.7	16.	77.	2.0	18.	79.
59	1.5	14.	74.	1.7	16.	76.
60	1.3	12.	71.	1.5	14.	74.
61	1.1	11.	67.	1.3	13.	71.
62	.97	9.5	64.	1.2	11.	68.
63	.85	8.5	61.	1.0	9.9	65.
64	.76	7.6	58.	.87	8.6	62.
65	.68	6.8	56.	.75	7.5	58.
66	.61	6.2	53.	.65	6.6	55.
67	.54	5.6	50.	.57	5.9	52.
68	.48	5.0	47.	.53	5.4	50.
69	.42	4.4	44.	.51	5.2	48.
70	.37	3.9	41.	.49	5.0	48.
71	.32	3.4	37.	.46	4.7	46.
72	.28	3.0	34.	.41	4.2	43.
73	.24	2.6	31.	.34	3.6	39.
74	.21	2.2	28.	.29	3.1	35.
75	.18	1.9	25.	.25	2.6	31.
76	.15	1.6	22.	.21	2.2	28.
77	.13	1.4	20.	.18	1.9	25.
78	.11	1.2	17.	.16	1.7	23.
79	.095	1.0	15.	.14	1.5	20.
80	.081	.87	13.	.12	1.3	18.
81	.072	.77	12.	.11	1.1	16.
82	.067	.72	11.	.095	1.0	15.
83	.064	.69	11.	.086	.92	14.
84	.061	.66	10.	.078	.83	13.
85	.058	.63	9.8	.072	.77	12.

Table PC-1-A-60. Chronic Granulocytic Leukemia Following
Exposure at Age 60, by Age A_2 at Diagnosis, Sex, and Dose
in Rad of Low-LET Radiation. PC in Percent, to Two
Significant Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose			Dose		
	1	10	100	1	10	100
62	.57	5.9	52.	.68	6.9	56.
63	1.4	13.	73.	1.7	15.	76.
64	1.6	15.	75.	1.8	17.	78.
65	1.6	15.	75.	1.7	16.	77.
66	1.5	14.	74.	1.6	15.	75.
67	1.3	13.	72.	1.4	13.	72.
68	1.2	11.	69.	1.3	12.	71.
69	1.0	10.	66.	1.2	12.	70.
70	.90	8.9	63.	1.2	11.	69.
71	.77	7.8	59.	1.1	11.	67.
72	.67	6.7	55.	.95	9.3	64.
73	.57	5.8	51.	.79	7.9	60.
74	.48	4.9	47.	.66	6.7	55.
75	.41	4.2	43.	.55	5.7	51.
76	.34	3.6	39.	.47	4.8	46.
77	.29	3.1	35.	.40	4.1	42.
78	.25	2.6	31.	.34	3.5	39.
79	.20	2.1	27.	.29	3.0	35.
80	.17	1.8	24.	.25	2.7	32.
81	.15	1.6	22.	.22	2.3	29.
82	.14	1.5	21.	.20	2.1	27.
83	.13	1.4	20.	.17	1.8	24.
84	.12	1.3	19.	.16	1.7	23.
85	.12	1.3	18.	.14	1.5	21.
86	.11	1.2	17.	.14	1.4	20.
87	.11	1.1	16.	.13	1.4	19.
88	.10	1.1	16.	.12	1.3	18.
89	.095	1.0	15.	.12	1.2	18.
90	.090	.96	14.	.11	1.2	17.
91	.086	.92	14.	.10	1.1	16.
92	.082	.87	13.	.099	1.1	16.
93	.078	.83	13.	.095	1.0	15.
94	.074	.79	12.	.090	.96	14.
95	.071	.76	12.	.086	.92	14.

Table PC-1-A-70. Chronic Granulocytic Leukemia Following
    Exposure at Age 70, by Age A_2 at Diagnosis, Sex, and Dose
    in Rad of Low-LET Radiation. PC in Percent, to Two
    Significant Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
72	.37	3.9	41.	.53	5.4	50.
73	.90	8.9	63.	1.2	12.	70.
74	.98	9.6	65.	1.3	13.	71.
75	.91	9.0	63.	1.2	12.	70.
76	.80	8.0	60.	1.1	10.	67.
77	.69	7.0	56.	.92	9.1	63.
78	.58	5.9	52.	.79	7.9	59.
79	.47	4.9	47.	.67	6.8	55.
80	.40	4.1	42.	.58	5.9	52.
81	.34	3.6	39.	.50	5.1	48.
82	.31	3.3	37.	.43	4.5	45.
83	.29	3.0	35.	.38	4.0	41.
84	.27	2.8	33.	.34	3.5	38.
85	.25	2.6	32.	.30	3.2	36.
86	.23	2.5	30.	.28	3.0	34.
87	.22	2.3	29.	.26	2.8	33.
88	.21	2.2	28.	.25	2.6	31.
89	.19	2.0	26.	.23	2.4	30.
90	.18	1.9	25.	.22	2.3	29.
91	.17	1.8	24.	.20	2.2	27.
92	.16	1.7	23.	.19	2.0	26.
93	.15	1.6	22.	.18	1.9	25.
94	.14	1.5	21.	.17	1.8	24.
95	.13	1.4	20.	.16	1.7	23.
96	.13	1.4	19.	.15	1.6	22.
97	.12	1.3	18.	.15	1.5	21.
98	.11	1.2	17.	.14	1.5	20.
99	.11	1.2	17.	.13	1.4	19.
100	.10	1.1	16.	.12	1.3	19.
101	.098	1.0	15.	.12	1.3	18.
102	.093	1.0	15.	.11	1.2	17.
103	.089	.95	14.	.11	1.1	17.
104	.085	.91	14.	.10	1.1	16.
105	.081	.87	13.	.098	1.0	15.

Table PC-1-B-0. Acute Leukemia Following Exposure at Age 0, by Age A_2 at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
2	1.5	14.	74.	1.2	11.	69.
3	6.9	45.	93.	5.4	38.	91.
4	9.9	54.	95.	7.8	48.	94.
5	11.	58.	96.	8.8	51.	95.
6	12.	59.	96.	9.3	52.	95.
7	12.	58.	96.	9.0	51.	95.
8	10.	55.	95.	8.1	49.	94.
9	9.0	52.	95.	7.2	46.	94.
10	7.9	48.	94.	6.5	43.	93.
11	6.7	44.	93.	5.8	40.	92.
12	5.7	39.	92.	5.1	37.	91.
13	4.7	35.	90.	4.6	34.	90.
14	3.8	30.	88.	4.1	32.	89.
15	3.1	26.	86.	3.7	29.	88.
16	2.6	22.	83.	3.3	27.	86.
17	2.2	19.	80.	2.9	24.	85.
18	1.9	17.	78.	2.4	21.	82.
19	1.8	16.	77.	1.9	18.	79.
20	1.7	15.	76.	1.6	15.	75.
21	1.5	14.	74.	1.3	12.	71.
22	1.3	13.	71.	1.1	11.	67.
23	1.1	11.	68.	.95	9.3	64.
24	.95	9.4	64.	.82	8.1	60.
25	.81	8.0	60.	.71	7.1	57.
26	.68	6.9	56.	.61	6.2	53.
27	.58	6.0	52.	.53	5.5	50.
28	.50	5.1	48.	.47	4.8	46.
29	.43	4.4	44.	.41	4.2	43.
30	.37	3.9	41.	.36	3.7	40.
31	.32	3.3	37.	.31	3.2	36.
32	.28	2.9	34.	.26	2.7	32.
33	.24	2.5	31.	.22	2.3	29.
34	.21	2.2	28.	.18	2.0	25.
35	.18	1.9	25.	.16	1.7	22.

Table PC-1-B-10. Acute Leukemia Following Exposure at Age 10, by Age A_2 at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
12	1.0	10.	66.	.94	9.3	64.
13	5.6	39.	92.	5.5	39.	92.
14	8.1	49.	92.	8.8	51.	95.
15	8.3	49.	94.	9.8	54.	95.
16	7.6	47.	94.	9.8	54.	95.
17	6.8	44.	93.	8.8	51.	95.
18	6.1	41.	92.	7.5	47.	94.
19	5.6	39.	92.	6.1	41.	92.
20	5.2	37.	91.	5.0	36.	91.
21	4.7	35.	90.	4.1	31.	89.
22	4.1	31.	89.	3.4	27.	87.
23	3.4	27.	87.	2.9	24.	84.
24	2.8	24.	84.	2.4	21.	82.
25	2.3	21.	82.	2.1	18.	80.
26	2.0	18.	79.	1.8	16.	77.
27	1.6	15.	76.	1.5	14.	74.
28	1.4	13.	72.	1.3	12.	71.
29	1.2	11.	69.	1.1	11.	67.
30	.99	9.7	65.	.95	9.4	64.
31	.84	8.4	61.	.81	8.1	60.
32	.72	7.2	57.	.67	6.8	56.
33	.62	6.3	53.	.56	5.7	51.
34	.53	5.4	50.	.46	4.8	45.
35	.46	4.7	46.	.39	4.0	42.
36	.39	4.1	42.	.33	3.4	38.
37	.34	3.6	39.	.28	2.9	34.
38	.30	3.1	35.	.23	2.5	30.
39	.26	2.7	32.	.20	2.1	27.
40	.22	2.3	29.	.17	1.8	24.
41	.19	2.0	26.	.15	1.5	21.
42	.15	1.7	22.	.13	1.3	19.
43	.13	1.4	19.	.10	1.1	16.
44	.10	1.1	16.	.085	.90	14.
45	.086	.91	14.	.068	.73	11.

Table PC-1-B-20. Acute Leukemia Following Exposure at Age 20, by Age A_2 at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose			Dose		
	1	10	100	1	10	100
22	.35	3.7	40.	.29	3.0	35.
23	2.7	23.	84.	2.3	20.	81.
24	4.8	35.	90.	4.1	32.	89.
25	5.7	39.	92.	5.0	36.	91.
26	5.7	40.	92.	5.2	37.	91.
27	5.4	38.	91.	5.0	36.	91.
28	4.9	36.	90.	4.6	34.	90.
29	4.3	33.	89.	4.1	32.	89.
30	3.8	30.	88.	3.7	29.	88.
31	3.3	27.	86.	3.2	26.	86.
32	2.9	24.	85.	2.7	23.	84.
33	2.5	22.	82.	2.3	20.	81.
34	2.1	19.	80.	1.9	17.	78.
35	1.9	17.	78.	1.6	15.	75.
36	1.6	15.	75.	1.3	13.	71.
37	1.4	13.	72.	1.1	11.	68.
38	1.2	12.	69.	.96	9.4	64.
39	1.0	10.	66.	.81	8.1	60.
40	.90	9.0	63.	.69	7.0	56.
41	.76	7.6	59.	.59	6.0	52.
42	.63	6.4	54.	.51	5.2	49.
43	.51	5.3	49.	.42	4.4	44.
44	.42	4.3	44.	.34	3.6	39.
45	.34	3.6	39.	.27	2.9	34.
46	.28	3.0	35.	.22	2.3	29.
47	.24	2.5	31.	.19	2.0	26.
48	.20	2.1	27.	.16	1.7	23.
49	.17	1.8	24.	.14	1.5	21.
50	.15	1.6	21.	.13	1.4	19.
51	.13	1.3	19.	.11	1.2	17.
52	.11	1.2	17.	.10	1.1	16.
53	.093	1.0	15.	.086	.92	14.
54	.080	.86	13.	.074	.79	12.
55	.068	.73	11.	.063	.68	10.

Table PC-1-B-30. Acute Leukemia Following Exposure at Age 30, by Age A_2 at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
32	.070	.74	11.	.065	.70	11.
33	.82	8.2	60.	.74	7.5	58.
34	2.0	18.	79.	1.7	16.	77.
35	2.9	24.	85.	2.5	21.	82.
36	3.4	28.	87.	2.8	24.	84.
37	3.6	29.	87.	2.9	25.	85.
38	3.6	29.	87.	2.9	24.	85.
39	3.5	28.	87.	2.7	23.	84.
40	3.3	27.	86.	2.5	22.	83.
41	2.9	25.	85.	2.3	20.	81.
42	2.6	22.	83.	2.1	19.	80.
43	2.2	19.	81.	1.8	17.	77.
44	1.9	17.	78.	1.5	14.	74.
45	1.6	15.	75.	1.2	12.	70.
46	1.3	13.	71.	1.0	10.	66.
47	1.1	11.	68.	.89	8.9	62.
48	.98	9.6	65.	.79	7.9	60.
49	.85	8.4	61.	.72	7.2	57.
50	.74	7.4	58.	.65	6.6	55.
51	.64	6.5	54.	.59	6.0	52.
52	.56	5.7	51.	.52	5.3	49.
53	.49	5.0	48.	.45	4.7	46.
54	.43	4.4	44.	.39	4.1	42.
55	.37	3.8	40.	.34	3.5	39.
56	.31	3.2	37.	.29	3.0	35.
57	.26	2.7	32.	.24	2.6	31.
58	.21	2.3	28.	.20	2.2	27.
59	.18	1.9	25.	.17	1.8	24.
60	.15	1.6	21.	.15	1.6	21.
61	.12	1.3	19.	.13	1.3	19.
62	.11	1.1	16.	.11	1.2	17.
63	.091	.98	14.	.095	1.0	15.
64	.080	.86	13.	.083	.89	13.
65	.070	.75	11.	.073	.78	12.

Table PC-1-B-40. Acute Leukemia Following Exposure at Age 40, by Age A_2 at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
42	.008	.089	1.5	.006	.072	1.2
43	.16	1.6	22.	.13	1.4	19.
44	.50	5.1	48.	.41	4.2	43.
45	.88	8.7	62.	.69	7.0	56.
46	1.2	11.	69.	.92	9.1	63.
47	1.4	13.	72.	1.1	11.	67.
48	1.5	14.	74.	1.2	12.	69.
49	1.6	15.	74.	1.3	12.	71.
50	1.6	15.	74.	1.4	13.	72.
51	1.5	14.	74.	1.4	13.	72.
52	1.5	14.	73.	1.4	13.	72.
53	1.4	13.	72.	1.3	12.	71.
54	1.3	12.	71.	1.2	11.	69.
55	1.2	11.	69.	1.1	11.	67.
56	1.1	10.	66.	.98	9.6	65.
57	.93	9.2	63.	.87	8.6	62.
58	.80	8.0	60.	.76	7.6	59.
59	.69	7.0	56.	.67	6.8	56.
60	.60	6.1	53.	.59	6.0	52.
61	.52	5.3	49.	.53	5.4	49.
62	.45	4.7	46.	.47	4.8	47.
63	.41	4.2	43.	.42	4.3	44.
64	.36	3.8	40.	.38	3.9	41.
65	.33	3.4	38.	.34	3.5	38.
66	.29	3.1	35.	.30	3.2	36.
67	.26	2.7	32.	.27	2.9	33.
68	.22	2.3	29.	.24	2.5	31.
69	.19	2.0	26.	.21	2.2	28.
70	.16	1.7	23.	.18	1.9	25.
71	.13	1.4	20.	.16	1.7	23.
72	.12	1.2	18.	.14	1.5	21.
73	.10	1.1	16.	.12	1.3	19.
74	.088	.94	14.	.11	1.2	17.
75	.077	.83	13.	.098	1.0	15.

Table PC-1-B-50. Acute Leukemia Following Exposure at Age 50,
by Age A_2 at Diagnosis, Sex, and Dose in Rad of Low-LET
Radiation. PC in Percent, to Two Significant Digits or
Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose			Dose		
	1	10	100	1	10	100
52	.000	.004	.081	.000	.004	.071
53	.016	.17	2.9	.014	.15	2.5
54	.081	.86	13.	.071	.75	12.
55	.19	2.1	26.	.17	1.8	24.
56	.33	3.4	38.	.29	3.0	35.
57	.45	4.6	45.	.40	4.1	43.
58	.54	5.6	50.	.49	5.1	48.
59	.61	6.2	53.	.56	5.8	51.
60	.65	6.6	55.	.62	6.3	53.
61	.68	6.9	56.	.66	6.6	55.
62	.69	7.0	56.	.68	6.8	56.
63	.70	7.1	57.	.69	6.9	56.
64	.70	7.1	57.	.69	6.9	56.
65	.70	7.0	56.	.68	7.0	56.
66	.68	6.9	56.	.67	6.9	56.
67	.65	6.6	55.	.65	6.8	55.
68	.60	6.1	53.	.62	6.6	55.
69	.54	5.6	50.	.58	6.3	53.
70	.49	5.0	47.	.53	5.9	52.
71	.43	4.5	45.	.49	5.4	50.
72	.39	4.1	42.	.45	5.0	48.
73	.36	3.7	40.	.42	4.7	46.
74	.33	3.4	38.	.39	4.4	44.
75	.30	3.2	36.	.36	4.1	42.
76	.28	2.9	34.	.34	3.8	40.
77	.26	2.7	32.	.31	3.5	38.
78	.24	2.5	30.	.28	3.3	37.
79	.22	2.3	29.	.25	3.0	34.
80	.20	2.2	27.	.23	2.7	32.
81	.19	2.0	26.	.21	2.4	30.
82	.18	1.9	25.	.20	2.2	28.
83	.17	1.8	24.	.19	2.1	27.
84	.16	1.7	23.	.18	2.0	26.
85	.16	1.6	22.	.17	1.9	24.

Table PC-1-B-60. Acute Leukemia Following Exposure at Age 60,
   by Age A_2 at Diagnosis, Sex, and Dose in Rad of Low-LET
   Radiation. PC in Percent, to Two Significant Digits or
   Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
62	.000	.000	.002	.000	.000	.002
63	.001	.011	.19	.000	.009	.17
64	.008	.088	1.5	.007	.077	1.3
65	.028	.30	4.9	.025	.26	4.3
66	.062	.67	10.	.055	.59	9.3
67	.11	1.2	17.	.098	1.0	15.
68	.16	1.7	23.	.15	1.6	21.
69	.21	2.2	28.	.20	2.1	27.
70	.25	2.6	32.	.25	2.6	31.
71	.29	3.0	35.	.29	3.0	35.
72	.32	3.3	37.	.33	3.5	38.
73	.35	3.6	39.	.37	3.9	41.
74	.38	3.9	41.	.40	4.2	43.
75	.40	4.1	42.	.43	4.4	44.
76	.41	4.3	43.	.45	4.7	46.
77	.43	4.4	44.	.47	4.8	47.
78	.44	4.5	45.	.47	4.9	47.
79	.45	4.6	45.	.46	4.8	46.
80	.45	4.7	46.	.45	4.7	46.
81	.46	4.7	46.	.45	4.6	45.
82	.46	4.8	46.	.46	4.7	46.
83	.47	4.8	46.	.46	4.8	46.
84	.48	4.9	47.	.47	4.9	47.
85	.49	5.0	47.	.48	5.0	47.
86	.50	5.1	48.	.50	5.1	48.
87	.51	5.3	49.	.51	5.3	49.
88	.53	5.4	49.	.53	5.4	49.
89	.54	5.5	50.	.54	5.5	50.
90	.55	5.6	50.	.55	5.6	50.
91	.56	5.7	51.	.55	5.7	51.
92	.56	5.7	51.	.56	5.7	51.
93	.57	5.8	51.	.57	5.8	51.
94	.57	5.9	52.	.57	5.8	52.
95	.58	5.9	52.	.58	5.9	52.

Table PC-1-B-70. Acute Leukemia Following Exposure at Age 70, by Age A_2 at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose			Dose		
	1	10	100	1	10	100
72	.000	.000	.000	.000	.000	.000
73	.000	.000	.011	.000	.000	.010
74	.000	.008	.15	.000	.008	.14
75	.003	.042	.72	.003	.040	.69
76	.012	.13	2.1	.011	.12	2.0
77	.026	.28	4.6	.025	.27	4.4
78	.049	.52	8.2	.046	.49	7.8
79	.080	.85	13.	.073	.78	12.
80	.12	1.3	18.	.11	1.1	16.
81	.17	1.8	24.	.14	1.5	21.
82	.22	2.4	29.	.19	2.0	26.
83	.29	3.0	35.	.25	2.6	32.
84	.36	3.8	40.	.32	3.3	37.
85	.45	4.6	45.	.39	4.1	42.
86	.54	5.6	50.	.48	4.9	47.
87	.65	6.6	55.	.57	5.8	51.
88	.76	7.7	59.	.67	6.8	55.
89	.88	8.8	62.	.78	7.8	59.
90	1.0	9.9	65.	.89	8.8	62.
91	1.1	11.	68.	1.0	9.8	65.
92	1.3	12.	70.	1.1	11.	68.
93	1.4	13.	73.	1.2	12.	70.
94	1.6	15.	74.	1.4	13.	72.
95	1.7	16.	76.	1.5	14.	74.
96	1.8	17.	78.	1.6	15.	75.
97	2.0	18.	79.	1.7	16.	77.
98	2.1	19.	80.	1.9	17.	78.
99	2.3	20.	81.	2.0	18.	79.
100	2.4	21.	82.	2.1	19.	80.
101	2.5	22.	83.	2.2	20.	81.
102	2.7	23.	84.	2.4	21.	82.
103	2.8	24.	84.	2.5	22.	82.
104	3.0	25.	85.	2.6	22.	83.
105	3.1	26.	85.	2.7	23.	84.

Table PC-1-C-0. Leukemia Excluding CLL Following Exposure
    at Age 0, by Age A_2 at Diagnosis, Sex, and Dose in Rad
    of Low-LET Radiation. PC in Percent, to Two Significant
    Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
2	2.1	19.	80.	1.6	15.	76.
3	8.5	50.	94.	6.7	44.	93.
4	12.	59.	96.	9.5	53.	95.
5	14.	63.	97.	11.	56.	96.
6	14.	65.	97.	11.	58.	96.
7	14.	64.	97.	11.	57.	96.
8	13.	62.	97.	10.	55.	95.
9	12.	59.	96.	9.5	53.	95.
10	11.	56.	96.	8.8	51.	95.
11	9.5	53.	95.	8.1	49.	94.
12	8.3	49.	94.	7.4	46.	94.
13	7.1	45.	93.	6.8	44.	93.
14	6.0	41.	92.	6.3	42.	93.
15	5.1	37.	91.	5.9	40.	92.
16	4.4	33.	90.	5.4	38.	91.
17	3.9	30.	88.	4.7	35.	90.
18	3.5	28.	87.	4.1	32.	89.
19	3.3	27.	86.	3.6	28.	87.
20	3.2	26.	86.	3.1	26.	85.
21	3.0	25.	85.	2.7	23.	84.
22	2.7	23.	84.	2.4	21.	82.
23	2.4	21.	82.	2.1	19.	80.
24	2.1	18.	79.	1.9	17.	78.
25	1.7	16.	77.	1.7	16.	76.
26	1.5	14.	74.	1.5	14.	74.
27	1.4	13.	72.	1.4	13.	72.
28	1.2	12.	70.	1.3	12.	70.
29	1.1	11.	68.	1.1	11.	68.
30	1.1	10.	67.	1.0	10.	66.
31	.99	9.7	65.	.93	9.2	63.
32	.91	9.0	63.	.83	8.3	61.
33	.83	8.3	61.	.74	7.4	58.
34	.76	7.6	59.	.66	6.6	55.
35	.70	7.1	57.	.59	6.0	52.

Table PC-1-C-10. Leukemia Excluding CLL Following Exposure
   at Age 10, by Age A_2 at Diagnosis, Sex, and Dose in Rad
   of Low-LET Radiation. PC in Percent, to Two Significant
   Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
12	1.7	16.	76.	1.5	14.	74.
13	7.3	46.	94.	7.0	45.	93.
14	10.	54.	95.	10.	56.	96.
15	10.	55.	95.	12.	58.	96.
16	9.3	53.	95.	11.	58.	96.
17	8.3	49.	94.	10.	55.	95.
18	7.5	46.	94.	8.6	50.	95.
19	6.8	44.	93.	7.3	46.	94.
20	6.3	42.	93.	6.2	42.	92.
21	5.7	39.	92.	5.2	37.	91.
22	5.0	36.	91.	4.4	33.	90.
23	4.2	32.	89.	3.8	30.	88.
24	3.4	28.	87.	3.2	26.	86.
25	2.8	24.	84.	2.8	23.	84.
26	2.3	20.	81.	2.4	21.	82.
27	2.0	18.	79.	2.0	18.	79.
28	1.7	16.	77.	1.8	16.	77.
29	1.6	15.	74.	1.6	15.	74.
30	1.4	13.	72.	1.4	13.	72.
31	1.2	12.	70.	1.2	11.	69.
32	1.1	11.	67.	1.0	9.9	65.
33	.98	9.6	65.	.87	8.6	62.
34	.87	8.6	62.	.75	7.5	58.
35	.77	7.7	59.	.65	6.6	55.
36	.69	7.0	56.	.57	5.8	51.
37	.62	6.3	53.	.50	5.1	48.
38	.55	5.7	51.	.44	4.5	45.
39	.50	5.1	48.	.39	4.0	42.
40	.45	4.6	45.	.35	3.6	39.
41	.40	4.1	43.	.31	3.2	36.
42	.36	3.7	40.	.28	2.9	34.
43	.32	3.3	37.	.25	2.6	31.
44	.28	2.9	34.	.22	2.3	29.
45	.24	2.5	31.	.19	2.0	26.

Table PC-1-C-20.   Leukemia Excluding CLL Following Exposure
   at Age 20, by Age A_2 at Diagnosis, Sex, and Dose in Rad
   of Low-LET Radiation.   PC in Percent, to Two Significant
   Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
22	.81	8.1	60.	.72	7.2	57.
23	3.6	29.	87.	3.2	26.	86.
24	5.4	38.	91.	5.0	36.	91.
25	5.8	40.	92.	5.7	40.	92.
26	5.6	39.	92.	5.7	39.	92.
27	5.2	37.	91.	5.3	38.	91.
28	4.8	35.	90.	4.8	35.	90.
29	4.3	33.	89.	4.3	33.	89.
30	3.9	30.	88.	3.8	30.	88.
31	3.5	28.	87.	3.3	27.	86.
32	3.1	25.	85.	2.8	24.	84.
33	2.7	23.	83.	2.4	21.	82.
34	2.3	20.	81.	2.0	18.	79.
35	2.0	18.	79.	1.7	16.	76.
36	1.8	16.	77.	1.5	14.	73.
37	1.5	14.	74.	1.2	12.	70.
38	1.4	13.	72.	1.1	10.	67.
39	1.2	11.	69.	.93	9.2	63.
40	1.0	10.	66.	.81	8.0	60.
41	.91	9.0	63.	.70	7.1	57.
42	.79	7.9	60.	.61	6.2	53.
43	.68	6.9	56.	.53	5.4	50.
44	.58	5.9	52.	.45	4.7	46.
45	.49	5.1	48.	.39	4.0	42.
46	.42	4.3	44.	.33	3.5	38.
47	.36	3.8	40.	.29	3.0	35.
48	.31	3.3	37.	.25	2.6	32.
49	.27	2.8	33.	.22	2.3	29.
50	.23	2.5	30.	.20	2.1	27.
51	.20	2.1	27.	.17	1.8	24.
52	.18	1.9	25.	.16	1.7	22.
53	.15	1.6	22.	.14	1.5	20.
54	.13	1.4	20.	.12	1.3	18.
55	.12	1.2	18.	.11	1.2	17.

Table PC-1-C-30. Leukemia Excluding CLL Following Exposure
at Age 30, by Age A_2 at Diagnosis, Sex, and Dose in Rad
of Low-LET Radiation. PC in Percent, to Two Significant
Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
32	.47	4.8	46.	.43	4.4	44.
33	1.7	16.	76.	1.5	14.	74.
34	2.8	23.	84.	2.4	21.	82.
35	3.4	28.	87.	2.9	24.	85.
36	3.8	30.	88.	3.1	26.	86.
37	3.8	30.	88.	3.1	26.	85.
38	3.7	29.	88.	3.0	25.	85.
39	3.5	28.	87.	2.8	23.	84.
40	3.2	26.	86.	2.5	22.	83.
41	2.9	25.	85.	2.3	20.	81.
42	2.6	23.	83.	2.1	18.	80.
43	2.3	20.	82.	1.8	17.	77.
44	2.0	18.	79.	1.6	15.	75.
45	1.7	16.	77.	1.4	13.	72.
46	1.5	14.	74.	1.2	11.	69.
47	1.3	12.	71.	1.0	10.	66.
48	1.1	11.	67.	.90	8.9	63.
49	.96	9.5	64.	.79	7.9	60.
50	.83	8.3	61.	.70	7.1	57.
51	.72	7.3	57.	.62	6.3	54.
52	.63	6.4	54.	.55	5.6	51.
53	.54	5.6	50.	.49	5.0	47.
54	.47	4.8	47.	.43	4.4	44.
55	.40	4.2	43.	.38	3.9	41.
56	.34	3.6	39.	.33	3.4	38.
57	.29	3.0	35.	.28	3.0	34.
58	.24	2.5	31.	.25	2.6	31.
59	.20	2.1	27.	.21	2.2	28.
60	.17	1.8	24.	.18	1.9	25.
61	.15	1.6	21.	.16	1.7	23.
62	.13	1.4	19.	.14	1.5	20.
63	.11	1.2	17.	.12	1.3	18.
64	.099	1.1	15.	.11	1.1	16.
65	.087	.93	14.	.093	.99	15.

Table PC-1-C-40. Leukemia Excluding CLL Following Exposure
    at Age 40, by Age A_2 at Diagnosis, Sex, and Dose in Rad
    of Low-LET Radiation. PC in Percent, to Two Significant
    Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
42	.44	4.6	45.	.34	3.6	39.
43	1.2	12.	69.	.93	9.2	63.
44	1.6	15.	75.	1.2	12.	70.
45	1.8	17.	77.	1.4	14.	73.
46	1.9	18.	79.	1.5	14.	74.
47	2.0	18.	79.	1.6	15.	75.
48	2.0	18.	79.	1.6	15.	75.
49	1.9	17.	78.	1.6	15.	75.
50	1.8	16.	77.	1.5	14.	74.
51	1.7	16.	76.	1.5	14.	73.
52	1.6	15.	74.	1.4	13.	72.
53	1.4	14.	73.	1.3	12.	71.
54	1.3	12.	71.	1.2	11.	69.
55	1.2	11.	68.	1.1	11.	67.
56	1.0	10.	66.	.98	9.6	65.
57	.89	8.8	62.	.87	8.7	62.
58	.76	7.6	59.	.78	7.8	59.
59	.66	6.7	55.	.69	6.9	56.
60	.57	5.9	52.	.61	6.2	53.
61	.50	5.1	48.	.54	5.5	50.
62	.44	4.6	45.	.48	4.9	47.
63	.39	4.1	42.	.42	4.3	44.
64	.35	3.7	39.	.38	3.9	41.
65	.31	3.3	37.	.33	3.5	38.
66	.28	3.0	34.	.30	3.1	36.
67	.25	2.7	32.	.27	2.8	33.
68	.22	2.3	29.	.24	2.5	31.
69	.19	2.0	26.	.21	2.2	28.
70	.16	1.7	23.	.19	2.0	26.
71	.14	1.5	20.	.17	1.8	24.
72	.12	1.3	18.	.15	1.6	22.
73	.10	1.1	16.	.13	1.4	20.
74	.090	.96	14.	.12	1.2	18.
75	.079	.85	13.	.10	1.1	16.

Table PC-1-C-50. Leukemia Excluding CLL Following Exposure
at Age 50, by Age A_2 at Diagnosis, Sex, and Dose in Rad
of Low-LET Radiation. PC in Percent, to Two Significant
Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
52	.43	4.5	45.	.37	3.9	41.
53	1.1	10.	67.	.94	9.3	64.
54	1.2	12.	70.	1.1	11.	67.
55	1.2	12.	70.	1.1	11.	68.
56	1.2	11.	69.	1.1	11.	67.
57	1.1	11.	67.	1.1	10.	66.
58	1.0	9.8	65.	1.0	9.8	65.
59	.93	9.2	63.	.95	9.3	64.
60	.86	8.6	62.	.89	8.8	62.
61	.80	8.0	60.	.84	8.4	61.
62	.75	7.5	58.	.79	7.9	60.
63	.71	7.1	57.	.74	7.5	58.
64	.67	6.8	55.	.70	7.1	57.
65	.63	6.4	54.	.66	6.6	55.
66	.59	6.0	52.	.62	6.3	53.
67	.56	5.7	51.	.58	5.9	52.
68	.51	5.2	48.	.54	5.5	50.
69	.45	4.7	46.	.50	5.1	48.
70	.40	4.1	43.	.46	4.7	46.
71	.35	3.7	40.	.42	4.4	44.
72	.31	3.3	37.	.39	4.0	42.
73	.28	3.0	34.	.35	3.7	40.
74	.25	2.7	32.	.32	3.4	37.
75	.23	2.4	30.	.29	3.1	35.
76	.21	2.2	28.	.26	2.8	33.
77	.19	2.0	26.	.24	2.5	31.
78	.17	1.8	24.	.22	2.3	29.
79	.16	1.7	23.	.19	2.0	25.
80	.14	1.5	21.	.17	1.8	24.
81	.13	1.4	20.	.16	1.7	22.
82	.12	1.3	18.	.14	1.5	21.
83	.12	1.2	18.	.14	1.4	20.
84	.11	1.2	17.	.13	1.4	19.
85	.10	1.1	16.	.12	1.3	19.

Table PC-1-C-60. Leukemia Excluding CLL Following Exposure
at Age 60, by Age A_2 at Diagnosis, Sex, and Dose in Rad
of Low-LET Radiation. PC in Percent, to Two Significant
Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
62	.37	3.8	41.	.39	4.1	42.
63	.91	9.0	63.	.95	9.4	64.
64	1.0	10.	66.	1.1	11.	67.
65	1.0	9.8	65.	1.0	10.	66.
66	.92	9.0	63.	.95	9.4	64.
67	.83	8.3	61.	.86	8.6	62.
68	.73	7.3	58.	.77	7.7	59.
69	.63	6.4	54.	.69	6.9	56.
70	.54	5.5	50.	.61	6.2	53.
71	.46	4.8	46.	.55	5.6	51.
72	.40	4.2	43.	.50	5.1	48.
73	.36	3.7	40.	.45	4.6	46.
74	.32	3.3	37.	.41	4.2	43.
75	.29	3.0	35.	.37	3.8	41.
76	.26	2.8	33.	.34	3.5	38.
77	.24	2.6	31.	.31	3.2	36.
78	.22	2.4	29.	.28	2.9	34.
79	.21	2.2	28.	.25	2.7	32.
80	.19	2.0	26.	.23	2.4	30.
81	.18	1.9	25.	.21	2.2	28.
82	.17	1.8	24.	.20	2.1	27.
83	.16	1.7	23.	.19	2.0	26.
84	.16	1.7	23.	.19	2.0	26.
85	.16	1.6	22.	.18	1.9	25.
86	.15	1.6	22.	.18	1.9	25.
87	.15	1.6	22.	.18	1.9	25.
88	.15	1.6	22.	.18	1.9	25.
89	.15	1.6	22.	.18	1.9	25.
90	.15	1.6	22.	.18	1.9	25.
91	.15	1.6	22.	.18	1.9	24.
92	.15	1.6	21.	.17	1.8	24.
93	.15	1.6	21.	.17	1.8	24.
94	.15	1.5	21.	.17	1.8	24.
95	.14	1.5	21.	.17	1.8	24.

Table PC-1-C-70. Leukemia Excluding CLL Following Exposure
   at Age 70, by Age A_2 at Diagnosis, Sex, and Dose in Rad
   of Low-LET Radiation. PC in Percent, to Two Significant
   Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
72	.23	2.4	30.	.28	3.0	34.
73	.55	5.6	50.	.69	7.0	56.
74	.60	6.1	53.	.77	7.7	59.
75	.57	5.8	51.	.73	7.4	58.
76	.51	5.3	49.	.66	6.7	55.
77	.45	4.7	46.	.58	5.9	52.
78	.40	4.1	42.	.50	5.1	48.
79	.34	3.6	39.	.43	4.4	44.
80	.30	3.1	36.	.36	3.8	40.
81	.26	2.8	33.	.32	3.3	37.
82	.23	2.5	30.	.28	2.9	34.
83	.21	2.2	28.	.25	2.7	32.
84	.19	2.0	26.	.23	2.4	30.
85	.18	1.9	25.	.21	2.2	28.
86	.17	1.8	24.	.20	2.1	27.
87	.16	1.7	23.	.19	2.0	26.
88	.15	1.6	22.	.18	1.9	25.
89	.14	1.5	21.	.17	1.8	24.
90	.14	1.4	20.	.16	1.7	23.
91	.13	1.4	19.	.15	1.6	22.
92	.12	1.3	19.	.15	1.6	21.
93	.12	1.3	18.	.14	1.5	21.
94	.11	1.2	17.	.14	1.4	20.
95	.11	1.2	17.	.13	1.4	20.
96	.11	1.1	16.	.13	1.4	19.
97	.10	1.1	16.	.12	1.3	19.
98	.10	1.1	16.	.12	1.3	18.
99	.098	1.0	15.	.12	1.2	18.
100	.096	1.0	15.	.11	1.2	17.
101	.094	1.0	15.	.11	1.2	17.
102	.092	.98	15.	.11	1.2	17.
103	.091	.97	14.	.11	1.1	17.
104	.089	.95	14.	.11	1.1	16.
105	.088	.94	14.	.10	1.1	16.

Table PC-2-0. Bone and Joint Cancer Following Exposure at
   Age 0, by Age A_2 at Diagnosis, Sex, and Dose in Rad of
   Alpha Radiation. PC in Percent, to Two Significant Digits
   or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
1	.053	.53	5.1	.053	.53	5.1
2	15.	64.	95.	15.	64.	95.
3	46.	90.	99.	45.	89.	99.
4	57.	93.	99.	52.	92.	99.
5	56.	93.	99.	49.	91.	99.
6	51.	91.	99.	44.	89.	99.
7	44.	89.	99.	38.	86.	98.
8	34.	84.	98.	30.	81.	98.
9	24.	76.	97.	22.	74.	97.
10	17.	67.	95.	16.	66.	95.
11	12.	58.	93.	13.	59.	94.
12	9.5	51.	91.	10.	53.	92.
13	7.7	45.	89.	8.7	49.	90.
14	6.4	40.	87.	7.5	45.	89.
15	5.4	36.	85.	6.7	42.	88.
16	4.7	33.	83.	6.1	39.	87.
17	4.1	30.	81.	5.6	37.	86.
18	3.8	29.	80.	5.3	36.	85.
19	3.7	28.	79.	5.2	35.	84.
20	3.6	27.	79.	5.1	35.	84.
21	3.6	27.	79.	5.1	35.	84.
22	3.4	26.	78.	5.0	35.	84.
23	3.2	25.	77.	4.8	34.	84.
24	2.9	23.	75.	4.7	33.	83.
25	2.7	22.	74.	4.4	32.	82.
26	2.5	20.	72.	4.2	30.	81.
27	2.3	19.	70.	3.9	29.	80.
28	2.0	17.	67.	3.5	27.	78.
29	1.7	15.	64.	3.1	24.	76.
30	1.5	13.	61.	2.7	22.	73.
31	1.3	12.	58.	2.3	19.	71.
32	1.2	11.	55.	2.1	18.	68.
33	1.1	10.	53.	2.0	17.	68.
34	1.1	9.8	52.	2.1	18.	68.
35	1.0	9.4	51.	2.3	19.	70.

Table PC-2-10. Bone and Joint Cancer Following Exposure at
Age 10, by Age A_2 at Diagnosis, Sex, and Dose in Rad of
Alpha Radiation.[2] PC in Percent, to Two Significant Digits
or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
11	.004	.047	.47	.004	.049	.49
12	1.3	12.	57.	1.5	13.	60.
13	6.3	40.	87.	7.1	43.	88.
14	11.	54.	92.	13.	59.	93.
15	13.	60.	94.	16.	65.	95.
16	14.	61.	94.	17.	68.	95.
17	14.	61.	94.	18.	69.	96.
18	14.	61.	94.	18.	69.	96.
19	14.	61.	94.	18.	69.	96.
20	14.	61.	94.	19.	70.	96.
21	14.	61.	94.	19.	70.	96.
22	13.	60.	94.	19.	69.	96.
23	12.	58.	93.	18.	68.	96.
24	11.	56.	93.	17.	67.	95.
25	10.	54.	92.	16.	66.	95.
26	9.4	51.	91.	15.	64.	95.
27	8.5	48.	90.	14.	62.	94.
28	7.4	45.	89.	13.	59.	93.
29	6.4	41.	87.	11.	55.	92.
30	5.5	37.	85.	9.4	51.	91.
31	4.8	34.	84.	8.2	47.	90.
32	4.3	31.	82.	7.4	44.	89.
33	4.0	29.	80.	7.0	43.	88.
34	3.7	28.	79.	7.0	43.	88.
35	3.5	26.	78.	7.4	44.	89.
36	3.3	25.	77.	7.8	46.	89.
37	3.1	24.	76.	7.5	45.	89.
38	3.0	23.	75.	6.5	41.	87.
39	2.8	22.	74.	5.4	36.	85.
40	2.6	21.	73.	4.4	31.	82.
41	2.4	20.	71.	3.5	27.	78.
42	2.1	18.	68.	2.8	22.	74.
43	1.7	15.	63.	2.2	19.	70.
44	1.3	11.	56.	1.8	15.	64.
45	.94	8.6	49.	1.4	13.	59.

Table PC-2-20. Bone and Joint Cancer Following Exposure at
   Age 20, by Age A_2 at Diagnosis, Sex, and Dose in Rad of
   Alpha Radiation. PC in Percent, to Two Significant Digits
   or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
21	.005	.053	.53	.007	.079	.78
22	1.9	16.	66.	2.9	23.	75.
23	10.	53.	92.	15.	64.	95.
24	18.	69.	96.	27.	78.	97.
25	23.	75.	97.	33.	83.	98.
26	25.	77.	97.	37.	85.	98.
27	25.	77.	97.	37.	86.	98.
28	24.	76.	97.	36.	85.	98.
29	22.	74.	97.	34.	84.	98.
30	20.	71.	96.	31.	82.	98.
31	18.	68.	96.	28.	79.	97.
32	16.	66.	95.	25.	77.	97.
33	15.	64.	95.	24.	76.	97.
34	14.	62.	94.	24.	76.	97.
35	13.	60.	94.	25.	77.	97.
36	12.	58.	93.	26.	78.	97.
37	11.	56.	93.	25.	76.	97.
38	11.	54.	92.	21.	73.	96.
39	10.	53.	92.	18.	69.	96.
40	9.2	50.	91.	15.	63.	95.
41	8.4	48.	90.	12.	58.	93.
42	7.3	44.	89.	9.5	51.	91.
43	5.8	38.	86.	7.6	45.	89.
44	4.3	31.	82.	6.0	39.	86.
45	3.2	25.	77.	4.7	33.	83.
46	2.4	20.	71.	3.8	28.	80.
47	2.0	17.	67.	3.1	24.	76.
48	1.6	14.	63.	2.7	22.	74.
49	1.4	12.	58.	2.5	20.	72.
50	1.2	11.	54.	2.3	19.	70.
51	1.0	9.2	50.	2.0	17.	68.
52	.85	7.9	46.	1.7	15.	63.
53	.73	6.8	42.	1.3	12.	58.
54	.62	5.9	38.	1.1	9.9	52.
55	.53	5.1	35.	.88	8.2	47.

Table PC-2-30. Bone and Joint Cancer Following Exposure at Age 30, by Age A_2 at Diagnosis, Sex, and Dose in Rad of Alpha Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
31	.007	.072	.72	.013	.13	1.3
32	2.4	20.	71.	4.2	30.	81.
33	12.	58.	93.	20.	72.	96.
34	22.	73.	97.	36.	85.	98.
35	28.	79.	97.	46.	90.	99.
36	31.	82.	98.	53.	92.	99.
37	32.	82.	98.	54.	92.	99.
38	32.	82.	98.	52.	92.	99.
39	31.	82.	98.	48.	90.	99.
40	30.	81.	98.	42.	88.	99.
41	28.	79.	97.	36.	85.	98.
42	25.	77.	97.	31.	82.	98.
43	20.	72.	96.	26.	78.	97.
44	16.	65.	95.	21.	73.	96.
45	12.	57.	93.	17.	67.	95.
46	9.1	50.	91.	14.	62.	94.
47	7.3	44.	89.	11.	56.	93.
48	6.1	39.	87.	9.8	52.	92.
49	5.1	35.	84.	8.9	49.	91.
50	4.3	31.	82.	8.1	47.	90.
51	3.6	27.	79.	7.2	44.	89.
52	3.0	24.	76.	5.9	38.	86.
53	2.5	21.	72.	4.6	33.	83.
54	2.1	18.	68.	3.7	28.	79.
55	1.8	15.	65.	3.0	23.	75.
56	1.5	13.	61.	2.4	20.	71.
57	1.3	12.	57.	2.0	17.	67.
58	1.1	10.	53.	1.6	14.	62.
59	1.0	9.2	50.	1.3	12.	57.
60	.91	8.4	48.	1.1	10.	53.
61	.81	7.6	45.	.92	8.5	48.
62	.70	6.6	41.	.77	7.2	44.
63	.58	5.5	37.	.67	6.3	40.
64	.48	4.6	32.	.61	5.8	38.
65	.39	3.8	28.	.58	5.5	37.

Table PC-2-40. Bone and Joint Cancer Following Exposure at Age 40, by Age A_2 at Diagnosis, Sex, and Dose in Rad of Alpha Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
41	.013	.13	1.2	.019	.19	1.9
42	4.0	29.	80.	5.4	36.	85.
43	17.	67.	95.	21.	73.	96.
44	24.	76.	97.	31.	82.	98.
45	25.	77.	97.	34.	84.	98.
46	24.	76.	97.	34.	84.	98.
47	22.	74.	97.	32.	82.	98.
48	20.	71.	96.	30.	81.	98.
49	18.	68.	96.	28.	80.	98.
50	15.	64.	95.	27.	79.	97.
51	13.	60.	94.	24.	76.	97.
52	11.	56.	93.	21.	72.	96.
53	9.6	51.	91.	17.	67.	95.
54	8.1	47.	90.	14.	61.	94.
55	6.8	42.	88.	11.	55.	93.
56	5.7	38.	86.	9.0	50.	91.
57	4.8	34.	84.	7.3	44.	89.
58	4.2	30.	81.	5.9	39.	86.
59	3.6	27.	79.	4.8	34.	84.
60	3.2	25.	77.	4.0	29.	81.
61	2.9	23.	75.	3.3	25.	77.
62	2.4	20.	71.	2.7	22.	74.
63	2.0	17.	67.	2.3	19.	70.
64	1.6	14.	62.	2.1	18.	68.
65	1.3	12.	57.	1.9	16.	66.
66	1.1	9.7	52.	1.8	15.	64.
67	.88	8.1	47.	1.5	14.	61.
68	.74	6.9	43.	1.3	12.	57.
69	.62	5.9	38.	1.1	9.8	52.
70	.53	5.0	35.	.90	8.4	48.
71	.45	4.3	31.	.76	7.1	43.
72	.38	3.7	28.	.64	6.0	39.
73	.31	3.0	24.	.53	5.1	35.
74	.25	2.4	20.	.45	4.3	31.
75	.20	2.0	17.	.38	3.6	27.

Table PC-2-50. Bone and Joint Cancer Following Exposure at Age 50, by Age A_2 at Diagnosis, Sex, and Dose in Rad of Alpha Radiation.[2] PC in Percent, to Two Significant Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose			Dose		
	1	10	100	1	10	100
51	.004	.048	.48	.011	.11	1.0
52	1.5	13.	60.	3.2	25.	76.
53	7.3	44.	89.	14.	61.	94.
54	12.	59.	93.	21.	73.	96.
55	15.	64.	95.	24.	76.	97.
56	15.	65.	95.	23.	75.	97.
57	15.	63.	95.	22.	73.	97.
58	14.	61.	94.	19.	71.	96.
59	13.	59.	94.	17.	67.	95.
60	12.	57.	93.	14.	63.	94.
61	10.	54.	92.	12.	58.	93.
62	8.9	49.	91.	10.	53.	92.
63	7.3	44.	89.	8.8	49.	91.
64	5.9	39.	86.	7.9	46.	90.
65	4.8	33.	83.	7.3	44.	89.
66	3.9	29.	80.	6.6	41.	88.
67	3.2	25.	77.	5.7	38.	86.
68	2.6	21.	73.	4.7	33.	83.
69	2.2	18.	69.	3.9	29.	80.
70	1.8	16.	65.	3.2	25.	77.
71	1.5	13.	61.	2.6	21.	73.
72	1.3	11.	56.	2.2	18.	69.
73	1.0	9.5	51.	1.8	16.	65.
74	.81	7.6	45.	1.5	13.	60.
75	.64	6.0	39.	1.2	11.	56.
76	.52	4.9	34.	1.0	9.5	51.
77	.43	4.2	30.	.87	8.0	47.
78	.40	3.8	29.	.76	7.1	43.
79	.40	3.8	29.	.68	6.4	41.
80	.41	4.0	29.	.63	5.9	39.
81	.43	4.1	30.	.56	5.4	36.
82	.39	3.8	28.	.49	4.7	33.
83	.33	3.2	25.	.41	3.9	29.
84	.27	2.7	21.	.32	3.1	24.
85	.23	2.2	18.	.25	2.5	20.

Table PC-2-60. Bone and Joint Cancer Following Exposure at
    Age 60, by Age A_2 at Diagnosis, Sex, and Dose in Rad of
    Alpha Radiation.[2] PC in Percent, to Two Significant Digits
    or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
61	.003	.035	.35	.004	.043	.42
62	1.1	10.	53.	1.3	12.	57.
63	5.4	36.	85.	6.6	41.	88.
64	9.0	50.	91.	12.	58.	93.
65	10.	54.	92.	16.	65.	95.
66	10.	54.	92.	17.	67.	95.
67	9.8	52.	92.	17.	67.	95.
68	8.8	49.	91.	15.	64.	95.
69	7.7	45.	89.	13.	60.	94.
70	6.6	41.	88.	11.	56.	93.
71	5.6	37.	86.	9.5	51.	91.
72	4.7	33.	83.	8.0	46.	90.
73	3.8	28.	80.	6.6	41.	88.
74	3.0	24.	75.	5.5	37.	85.
75	2.3	19.	70.	4.5	32.	82.
76	1.9	16.	65.	3.7	28.	79.
77	1.5	13.	61.	3.1	24.	76.
78	1.4	12.	58.	2.6	21.	73.
79	1.4	12.	58.	2.3	19.	71.
80	1.4	12.	59.	2.1	18.	68.
81	1.4	12.	59.	1.9	16.	66.
82	1.3	11.	56.	1.6	14.	62.
83	1.1	9.6	52.	1.3	12.	57.
84	.85	7.9	46.	1.0	9.3	51.
85	.70	6.6	41.	.78	7.3	44.
86	.61	5.8	38.	.69	6.5	41.
87	.54	5.1	35.	.60	5.7	38.
88	.47	4.5	32.	.53	5.1	35.
89	.42	4.0	29.	.47	4.5	32.
90	.37	3.6	27.	.41	4.0	29.
91	.32	3.2	25.	.37	3.5	27.
92	.29	2.8	22.	.32	3.1	25.
93	.26	2.5	20.	.29	2.8	22.
94	.23	2.2	19.	.26	2.5	20.
95	.20	2.0	17.	.23	2.2	19.

Table PC-2-70. Bone and Joint Cancer Following Exposure at
    Age 70, by Age A_2 at Diagnosis, Sex, and Dose in Rad of
    Alpha Radiation. PC in Percent, to Two Significant Digits
    or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
71	.001	.018	.18	.003	.030	.30
72	.57	5.4	36.	.95	8.7	49.
73	2.8	22.	74.	4.6	33.	83.
74	4.6	32.	83.	8.0	46.	90.
75	5.2	35.	85.	9.4	51.	91.
76	5.2	35.	84.	9.6	52.	91.
77	4.9	34.	84.	9.0	50.	91.
78	4.7	33.	83.	8.4	48.	90.
79	4.8	34.	84.	7.8	46.	89.
80	5.0	35.	84.	7.2	44.	89.
81	5.1	35.	84.	6.5	41.	87.
82	4.6	33.	83.	5.6	37.	86.
83	3.8	29.	80.	4.6	32.	83.
84	3.1	24.	76.	3.5	27.	79.
85	2.5	21.	72.	2.7	22.	74.
86	2.2	18.	69.	2.4	19.	71.
87	1.9	16.	66.	2.0	17.	68.
88	1.6	14.	62.	1.8	15.	64.
89	1.4	13.	59.	1.5	13.	61.
90	1.2	11.	55.	1.3	12.	57.
91	1.1	9.7	52.	1.2	10.	54.
92	.93	8.5	48.	1.0	9.2	50.
93	.81	7.5	45.	.87	8.1	47.
94	.70	6.6	42.	.76	7.1	43.
95	.62	5.8	38.	.67	6.3	40.
96	.54	5.2	35.	.59	5.6	37.
97	.47	4.6	32.	.51	4.9	34.
98	.42	4.0	30.	.45	4.3	31.
99	.37	3.6	27.	.40	3.8	29.
100	.32	3.2	25.	.35	3.4	26.
101	.29	2.8	22.	.31	3.0	24.
102	.25	2.5	20.	.28	2.7	22.
103	.23	2.2	18.	.24	2.4	20.
104	.20	2.0	17.	.22	2.1	18.
105	.18	1.8	15.	.19	1.9	16.

Table PC-3. Salivary Gland Cancer 10 or More Years After
Exposure to Low-LET Radiation, by Age A_1 at Exposure,
Sex, and Dose in Rad. PC in Percent, to Two Significant
Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
0	4.9	36.	90.	4.3	33.	89.
1	4.5	34.	90.	4.0	31.	88.
2	4.2	32.	89.	3.7	29.	88.
3	3.9	31.	88.	3.4	28.	87.
4	3.7	29.	88.	3.2	26.	86.
5	3.5	28.	87.	2.9	25.	85.
6	3.2	27.	86.	2.7	23.	84.
7	3.0	25.	85.	2.5	22.	83.
8	2.8	24.	84.	2.3	20.	82.
9	2.7	23.	83.	2.2	19.	80.
10	2.5	21.	82.	2.0	18.	79.
11	2.3	20.	81.	1.9	17.	78.
12	2.1	19.	80.	1.8	17.	77.
13	2.0	18.	79.	1.7	16.	76.
14	1.8	17.	77.	1.6	15.	75.

Table PC-4. Esophagus Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose			Dose		
	1	10	100	1	10	100
20	.21	2.2	28.	.56	5.8	51.
21	.19	2.0	26.	.50	5.1	48.
22	.17	1.8	23.	.44	4.6	45.
23	.15	1.6	21.	.40	4.1	42.
24	.13	1.4	20.	.36	3.7	40.
25	.12	1.3	18.	.32	3.4	37.
26	.11	1.2	17.	.29	3.0	35.
27	.10	1.1	16.	.26	2.8	33.
28	.091	.98	14.	.24	2.5	31.
29	.084	.90	13.	.22	2.3	29.
30	.078	.83	13.	.21	2.2	28.
31	.072	.77	12.	.19	2.0	26.
32	.067	.72	11.	.18	1.9	25.
33	.063	.67	10.	.17	1.8	24.
34	.059	.63	9.8	.16	1.7	23.
35	.056	.60	9.4	.15	1.6	22.
36	.053	.57	8.9	.15	1.6	21.
37	.050	.54	8.5	.14	1.5	21.
38	.048	.52	8.2	.14	1.5	20.
39	.046	.49	7.8	.13	1.4	20.
40	.044	.47	7.6	.13	1.4	19.
41	.043	.46	7.3	.13	1.4	19.
42	.041	.44	7.1	.13	1.3	19.
43	.041	.44	7.0	.12	1.3	19.
44	.041	.44	7.0	.13	1.4	19.
45	.041	.44	7.1	.13	1.4	19.
46	.042	.45	7.2	.13	1.4	20.
47	.043	.47	7.4	.14	1.5	20.
48	.045	.48	7.7	.15	1.5	21.
49	.047	.50	8.0	.15	1.6	22.
50	.049	.52	8.3	.16	1.7	23.
51	.051	.54	8.6	.17	1.8	24.
52	.053	.57	8.9	.18	1.9	24.
53	.056	.59	9.3	.18	1.9	25.
54	.058	.62	9.7	.19	2.0	26.
55	.061	.65	10.	.20	2.1	27.
56	.064	.68	10.	.21	2.2	28.
57	.065	.71	11.	.22	2.3	29.
58	.069	.74	11.	.23	2.4	30.
59	.072	.77	12.	.24	2.5	31.
60	.075	.81	12.	.25	2.6	31.

Table PC-4 (Continued). Esophagus Cancer 10 or More Years
    After Exposure to Low-LET Radiation, by Age A_1 at Exposure,
    Sex, and Dose in Rad. PC in Percent, to Two Significant
    Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
61	.079	.85	13.	.25	2.7	32.
62	.083	.88	13.	.26	2.7	33.
63	.085	.92	14.	.27	2.8	33.
64	.090	.96	14.	.27	2.8	33.
65	.093	.99	15.	.28	2.9	34.
66	.095	1.0	15.	.28	2.9	34.
67	.099	1.1	15.	.28	3.0	34.
68	.10	1.1	16.	.29	3.0	35.
69	.10	1.1	16.	.29	3.0	35.
70	.11	1.1	16.	.29	3.0	35.
71	.11	1.1	16.	.29	3.0	35.
72	.11	1.1	17.	.29	3.0	35.
73	.11	1.1	17.	.29	3.0	35.
74	.11	1.2	17.	.28	3.0	34.
75	.11	1.1	17.	.28	2.9	34.

Table PC-5. Stomach Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose			Dose		
	1	10	100	1	10	100
10	1.7	16.	76.	2.3	21.	82.
11	1.4	14.	73.	2.0	18.	79.
12	1.2	12.	70.	1.7	16.	77.
13	1.1	11.	67.	1.5	14.	74.
14	.99	9.8	65.	1.4	13.	73.
15	.91	9.0	63.	1.3	13.	71.
16	.83	8.2	61.	1.2	12.	70.
17	.75	7.5	58.	1.2	11.	69.
18	.69	6.9	56.	1.1	11.	67.
19	.62	6.3	54.	1.0	10.	66.
20	.57	5.8	51.	1.0	9.8	65.
21	.52	5.4	49.	.96	9.4	64.
22	.48	4.9	47.	.91	9.0	63.
23	.44	4.6	45.	.87	8.7	62.
24	.41	4.3	43.	.83	8.2	61.
25	.38	4.0	42.	.78	7.8	59.
26	.36	3.7	40.	.74	7.4	58.
27	.33	3.5	38.	.69	7.0	56.
28	.31	3.3	37.	.65	6.6	55.
29	.29	3.1	35.	.62	6.3	53.
30	.27	2.8	33.	.59	6.0	52.
31	.25	2.7	32.	.56	5.7	51.
32	.24	2.5	30.	.53	5.5	50.
33	.22	2.3	29.	.51	5.2	49.
34	.21	2.2	28.	.48	5.0	47.
35	.19	2.0	26.	.46	4.7	46.
36	.18	1.9	25.	.44	4.5	45.
37	.17	1.8	24.	.41	4.3	43.
38	.16	1.7	23.	.39	4.0	42.
39	.16	1.6	22.	.37	3.8	41.
40	.15	1.6	21.	.35	3.6	39.
41	.14	1.5	21.	.33	3.5	38.
42	.14	1.4	20.	.32	3.3	37.
43	.13	1.4	20.	.30	3.2	36.
44	.13	1.4	19.	.30	3.1	35.
45	.13	1.4	19.	.29	3.0	35.
46	.13	1.4	19.	.28	3.0	34.
47	.13	1.4	19.	.28	2.9	34.
48	.13	1.4	19.	.28	2.9	34.
49	.13	1.4	19.	.28	2.9	34.
50	.13	1.4	19.	.27	2.9	34.

Table PC-5 (Continued). Stomach Cancer 10 or More Years
   After Exposure to Low-LET Radiation, by Age A_1 at Exposure,
   Sex, and Dose in Rad. PC in Percent, to Two Significant
   Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
51	.13	1.4	19.	.27	2.9	34.
52	.13	1.4	19.	.27	2.8	33.
53	.13	1.4	20.	.27	2.8	33.
54	.13	1.4	20.	.27	2.8	33.
55	.14	1.4	20.	.27	2.8	33.
56	.14	1.5	20.	.27	2.8	33.
57	.14	1.5	20.	.27	2.8	33.
58	.14	1.5	21.	.27	2.8	33.
59	.14	1.5	21.	.27	2.8	33.
60	.14	1.5	21.	.27	2.8	33.
61	.14	1.5	21.	.27	2.8	33.
62	.14	1.5	21.	.27	2.8	33.
63	.14	1.5	21.	.27	2.8	33.
64	.14	1.5	21.	.27	2.8	33.
65	.14	1.5	21.	.27	2.8	33.
66	.14	1.5	21.	.27	2.8	33.
67	.14	1.5	21.	.27	2.8	33.
68	.15	1.5	21.	.27	2.8	33.
69	.15	1.5	21.	.27	2.8	33.
70	.15	1.5	21.	.27	2.8	33.
71	.15	1.5	21.	.26	2.8	33.
72	.15	1.5	21.	.26	2.8	33.
73	.15	1.6	21.	.26	2.7	33.
74	.15	1.6	21.	.26	2.7	32.
75	.15	1.6	21.	.26	2.7	32.

Table PC-6. Colon Cancer 10 or More Years After Exposure
to Low-LET Radiation, by Age A_1 at Exposure, Sex, and
Dose in Rad. PC in Percent, to Two Significant Digits or
Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
20	.17	1.8	24.	.15	1.6	22.
21	.16	1.7	22.	.14	1.5	21.
22	.15	1.5	21.	.13	1.4	20.
23	.13	1.4	20.	.13	1.3	19.
24	.12	1.3	19.	.12	1.3	18.
25	.12	1.2	18.	.11	1.2	17.
26	.11	1.1	16.	.10	1.1	16.
27	.099	1.1	15.	.095	1.0	15.
28	.091	.97	14.	.089	.95	14.
29	.084	.90	13.	.083	.88	13.
30	.078	.83	13.	.077	.83	13.
31	.072	.77	12.	.072	.77	12.
32	.067	.72	11.	.068	.73	11.
33	.062	.66	10.	.064	.68	11.
34	.058	.62	9.6	.060	.64	9.9
35	.053	.57	9.0	.056	.60	9.4
36	.050	.53	8.4	.053	.57	8.9
37	.046	.50	7.9	.050	.54	8.5
38	.043	.46	7.4	.047	.51	8.0
39	.040	.43	6.9	.045	.48	7.6
40	.038	.41	6.5	.042	.45	7.2
41	.036	.38	6.2	.040	.43	6.9
42	.034	.36	5.8	.038	.41	6.5
43	.032	.35	5.6	.036	.39	6.3
44	.051	.33	5.4	.035	.38	6.1
45	.030	.33	5.3	.034	.37	6.0
46	.030	.32	5.3	.034	.36	5.9
47	.030	.32	5.2	.033	.36	5.8
48	.030	.32	5.2	.033	.36	5.8
49	.030	.32	5.2	.033	.36	5.8
50	.030	.32	5.3	.034	.36	5.8
51	.030	.32	5.3	.034	.36	5.9
52	.030	.33	5.3	.034	.37	5.9
53	.031	.33	5.4	.034	.37	6.0
54	.031	.33	5.4	.035	.37	6.1
55	.031	.34	5.5	.035	.38	6.1
56	.032	.34	5.5	.036	.38	6.2
57	.032	.34	5.6	.036	.39	6.3
58	.032	.35	5.6	.037	.39	6.3
59	.032	.35	5.6	.037	.40	6.4
60	.033	.35	5.7	.038	.40	6.5

Table PC-6 (Continued). Colon Cancer 10 or More Years After
Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex,
and Dose in Rad. PC in Percent, to Two Significant Digits
or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
61	.033	.35	5.7	.038	.41	6.6
62	.033	.36	5.8	.038	.41	6.6
63	.033	.36	5.8	.039	.42	6.7
64	.033	.36	5.8	.039	.42	6.8
65	.034	.36	5.8	.040	.43	6.8
66	.034	.36	5.9	.040	.43	6.9
67	.034	.36	5.9	.041	.43	7.0
68	.034	.36	5.9	.041	.44	7.0
69	.034	.36	5.9	.041	.44	7.1
70	.034	.36	5.9	.042	.45	7.2
71	.034	.36	5.9	.042	.45	7.2
72	.034	.36	5.9	.042	.45	7.2
73	.034	.36	5.9	.042	.46	7.3
74	.034	.36	5.8	.043	.46	7.3
75	.033	.36	5.8	.043	.46	7.3

Table PC-7. Liver Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
20	2.8	23.	84.	4.8	35.	90.
21	2.4	21.	82.	4.5	33.	90.
22	2.1	19.	80.	4.1	32.	89.
23	1.9	17.	78.	3.8	30.	88.
24	1.7	16.	76.	3.4	28.	87.
25	1.5	14.	74.	3.1	26.	86.
26	1.3	13.	71.	2.9	24.	84.
27	1.2	11.	69.	2.6	22.	83.
28	1.1	10.	66.	2.4	21.	82.
29	.94	9.3	64.	2.2	20.	81.
30	.84	8.4	61.	2.0	18.	79.
31	.76	7.6	58.	1.9	17.	78.
32	.68	6.9	56.	1.7	16.	77.
33	.61	6.2	53.	1.6	15.	75.
34	.56	5.7	51.	1.5	14.	74.
35	.51	5.2	48.	1.4	13.	72.
36	.46	4.8	46.	1.3	12.	71.
37	.42	4.4	44.	1.2	11.	69.
38	.39	4.0	42.	1.1	11.	67.
39	.36	3.7	40.	1.0	10.	66.
40	.33	3.5	38.	.95	9.4	64.
41	.31	3.2	36.	.88	8.8	62.
42	.29	3.0	35.	.82	8.2	60.
43	.27	2.8	33.	.76	7.6	59.
44	.25	2.7	32.	.71	7.2	57.
45	.24	2.5	31.	.67	6.8	55.
46	.22	2.4	29.	.63	6.4	54.
47	.21	2.2	28.	.59	6.0	52.
48	.20	2.1	27.	.56	5.7	51.
49	.19	2.0	26.	.53	5.4	50.
50	.18	1.9	25.	.50	5.2	48.
51	.18	1.9	24.	.48	4.9	47.
52	.17	1.8	24.	.46	4.7	46.
53	.16	1.7	23.	.44	4.5	45.
54	.16	1.7	23.	.42	4.3	44.
55	.15	1.6	22.	.40	4.1	43.
56	.15	1.6	22.	.38	4.0	41.
57	.15	1.5	21.	.37	3.8	40.
58	.14	1.5	21.	.35	3.7	39.
59	.14	1.5	20.	.34	3.5	39.
60	.14	1.5	20.	.33	3.4	38.

Table PC-7 (Continued). Liver Cancer 10 or More Years After
Exposure to Low-LET Radiation, by Age A at Exposure, Sex,
Dose in Rad. PC in Percent, to Two Significant Digits or
Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
61	.13	1.4	20.	.32	3.3	37.
62	.13	1.4	20.	.31	3.2	37.
63	.13	1.4	19.	.30	3.2	36.
64	.13	1.4	19.	.30	3.1	35.
65	.13	1.4	19.	.29	3.0	35.
66	.13	1.4	19.	.28	3.0	35.
67	.13	1.4	19.	.28	2.9	34.
68	.13	1.4	19.	.27	2.9	34.
69	.13	1.4	19.	.27	2.8	33.
70	.13	1.4	19.	.26	2.8	33.
71	.13	1.4	19.	.26	2.7	32.
72	.13	1.4	19.	.26	2.7	32.
73	.13	1.4	19.	.25	2.7	32.
74	.13	1.4	20.	.25	2.6	32.
75	.13	1.4	20.	.25	2.6	31.

Table PC-8. Pancreas Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose			Dose		
	1	10	100	1	10	100
20	.45	4.6	45.	.74	7.4	58.
21	.40	4.2	43.	.67	6.7	55.
22	.36	3.8	40.	.60	6.1	53.
23	.33	3.4	38.	.54	5.5	50.
24	.30	3.1	35.	.48	4.9	47.
25	.27	2.8	33.	.43	4.5	44.
26	.25	2.6	31.	.39	4.0	42.
27	.23	2.4	30.	.35	3.7	39.
28	.21	2.2	28.	.32	3.3	37.
29	.19	2.0	26.	.29	3.0	35.
30	.18	1.9	25.	.27	2.8	33.
31	.16	1.7	23.	.25	2.6	31.
32	.15	1.6	22.	.23	2.4	30.
33	.14	1.5	21.	.21	2.2	28.
34	.13	1.4	20.	.20	2.1	27.
35	.12	1.3	19.	.19	2.0	26.
36	.12	1.2	18.	.17	1.8	24.
37	.11	1.2	17.	.16	1.7	23.
38	.10	1.1	16.	.15	1.6	22.
39	.099	1.1	15.	.15	1.5	21.
40	.094	1.0	15.	.14	1.5	20.
41	.090	.96	14.	.13	1.4	19.
42	.086	.92	14.	.12	1.3	19.
43	.084	.89	13.	.12	1.3	18.
44	.082	.88	13.	.12	1.3	18.
45	.082	.87	13.	.12	1.3	18.
46	.082	.87	13.	.12	1.2	18.
47	.082	.88	13.	.12	1.2	18.
48	.083	.88	13.	.12	1.3	18.
49	.084	.90	13.	.12	1.3	18.
50	.085	.91	14.	.12	1.3	18.
51	.087	.93	14.	.12	1.3	18.
52	.089	.95	14.	.12	1.3	19.
53	.091	.97	14.	.13	1.3	19.
54	.093	.99	15.	.13	1.4	19.
55	.095	1.0	15.	.13	1.4	19.
56	.097	1.0	15.	.13	1.4	20.
57	.099	1.1	15.	.13	1.4	20.
58	.10	1.1	16.	.14	1.5	20.
59	.10	1.1	16.	.14	1.5	21.
60	.10	1.1	16.	.14	1.5	21.

Table PC-8 (Continued). Pancreas Cancer 10 or More Years
    After Exposure to Low-LET Radiation, by Age A_1 at Exposure,
    Sex, and Dose in Rad. PC in Percent, to Two Significant
    Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
61	.11	1.1	16.	.15	1.6	21.
62	.11	1.1	17.	.15	1.6	21.
63	.11	1.2	17.	.15	1.6	22.
64	.11	1.2	17.	.15	1.6	22.
65	.11	1.2	17.	.15	1.6	22.
66	.11	1.2	18.	.16	1.7	22.
67	.12	1.2	18.	.16	1.7	23.
68	.12	1.3	18.	.16	1.7	23.
69	.12	1.3	18.	.16	1.7	23.
70	.12	1.3	18.	.17	1.8	23.
71	.12	1.3	18.	.17	1.8	24.
72	.12	1.3	18.	.17	1.8	24.
73	.12	1.3	18.	.17	1.8	24.
74	.12	1.3	18.	.17	1.8	24.
75	.12	1.3	18.	.17	1.8	24.

Table PC-9-A. Lung Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad, Given No Information on Smoking. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose			Dose		
	1	10	100	1	10	100
10	.39	4.0	42.	.56	5.7	51.
11	.35	3.7	39.	.51	5.2	49.
12	.31	3.3	37.	.47	4.8	46.
13	.28	2.9	34.	.42	4.4	44.
14	.24	2.6	31.	.38	4.0	42.
15	.22	2.3	28.	.35	3.7	39.
16	.19	2.0	26.	.32	3.3	37.
17	.17	1.8	24.	.29	3.1	35.
18	.15	1.6	22.	.27	2.8	33.
19	.14	1.5	20.	.25	2.6	32.
20	.12	1.3	19.	.23	2.4	30.
21	.11	1.2	17.	.22	2.3	28.
22	.10	1.1	16.	.20	2.1	27.
23	.093	.99	15.	.19	2.0	26.
24	.086	.91	14.	.18	1.9	24.
25	.079	.84	13.	.16	1.7	23.
26	.073	.78	12.	.16	1.6	22.
27	.067	.72	11.	.15	1.6	21.
28	.062	.67	10.	.14	1.5	20.
29	.058	.62	9.7	.13	1.4	20.
30	.054	.58	9.1	.13	1.3	19.
31	.051	.54	8.6	.12	1.3	18.
32	.048	.51	8.1	.12	1.2	18.
33	.045	.48	7.6	.11	1.2	17.
34	.042	.45	7.2	.11	1.1	17.
35	.040	.43	6.9	.10	1.1	16.
36	.038	.41	6.6	.10	1.1	16.
37	.036	.39	6.3	.10	1.1	16.
38	.035	.37	6.0	.099	1.1	15.
39	.033	.36	5.8	.098	1.0	15.
40	.032	.34	5.6	.096	1.0	15.
41	.031	.33	5.4	.096	1.0	15.
42	.030	.32	5.2	.095	1.0	15.
43	.029	.31	5.1	.095	1.0	15.
44	.028	.30	5.0	.095	1.0	15.
45	.028	.30	4.9	.095	1.0	15.
46	.027	.29	4.8	.096	1.0	15.
47	.027	.28	4.7	.097	1.0	15.
48	.026	.28	4.6	.098	1.0	15.
49	.026	.28	4.6	.099	1.1	15.
50	.026	.28	4.5	.10	1.1	16.

Table PC-9-A (Continued). Lung Cancer 10 or More Years After
Exposure to Low-LET Radiation, by Age A, at Exposure, Sex,
and Dose in Rad, Given No Information on Smoking. PC in
Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
51	.025	.27	4.5	.10	1.1	16.
52	.025	.27	4.5	.10	1.1	16.
53	.025	.27	4.4	.11	1.1	16.
54	.025	.27	4.4	.11	1.2	17.
55	.025	.27	4.5	.11	1.2	17.
56	.025	.27	4.5	.12	1.2	18.
57	.026	.27	4.5	.12	1.3	18.
58	.026	.28	4.5	.12	1.3	19.
59	.026	.28	4.6	.13	1.3	19.
60	.026	.28	4.6	.13	1.4	19.
61	.027	.29	4.7	.13	1.4	20.
62	.027	.29	4.8	.14	1.5	20.
63	.028	.30	4.9	.14	1.5	21.
64	.028	.30	5.0	.15	1.6	21.
65	.029	.31	5.1	.15	1.6	22.
66	.030	.32	5.2	.16	1.7	23.
67	.031	.33	5.4	.16	1.7	23.
68	.032	.35	5.6	.17	1.8	24.
69	.033	.36	5.8	.18	1.9	24.
70	.035	.37	6.0	.18	1.9	25.
71	.036	.39	6.2	.19	2.0	26.
72	.037	.40	6.4	.19	2.0	26.
73	.039	.42	6.7	.19	2.0	26.
74	.040	.43	6.9	.20	2.1	27.
75	.041	.44	7.1	.20	2.1	27.

Table PC-9-B. Lung Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad, for Nonsmokers. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose			Dose		
	1	10	100	1	10	100
10	2.6	22.	83.	2.5	22.	83.
11	2.3	21.	82.	2.3	20.	82.
12	2.1	19.	80.	2.1	19.	80.
13	1.9	17.	78.	1.9	18.	78.
14	1.6	15.	75.	1.8	16.	77.
15	1.4	14.	73.	1.6	15.	75.
16	1.3	12.	71.	1.5	14.	73.
17	1.1	11.	68.	1.3	13.	72.
18	1.0	10.	66.	1.2	12.	70.
19	.93	9.1	63.	1.1	11.	68.
20	.83	8.3	61.	1.1	10.	67.
21	.76	7.6	58.	.99	9.7	65.
22	.69	7.0	56.	.92	9.1	63.
23	.63	6.4	54.	.86	8.6	62.
24	.58	5.9	52.	.81	8.1	60.
25	.53	5.5	50.	.76	7.6	58.
26	.49	5.1	48.	.72	7.2	57.
27	.46	4.7	46.	.67	6.8	56.
28	.42	4.4	44.	.64	6.5	54.
29	.39	4.1	42.	.61	6.2	53.
30	.37	3.8	41.	.58	5.9	52.
31	.34	3.6	39.	.56	5.7	51.
32	.32	3.4	37.	.54	5.5	50.
33	.30	3.2	36.	.52	5.3	49.
34	.29	3.0	35.	.50	5.1	48.
35	.27	2.9	33.	.48	5.0	47.
36	.26	2.7	32.	.48	4.9	47.
37	.25	2.6	31.	.46	4.8	46.
38	.24	2.5	30.	.46	4.7	46.
39	.23	2.4	30.	.45	4.7	46.
40	.22	2.3	29.	.45	4.6	45.
41	.21	2.2	28.	.44	4.6	45.
42	.20	2.1	27.	.44	4.5	45.
43	.20	2.1	27.	.44	4.5	45.
44	.19	2.0	26.	.44	4.5	45.
45	.19	2.0	26.	.44	4.5	45.
46	.18	1.9	25.	.44	4.6	45.
47	.18	1.9	25.	.45	4.6	45.
48	.18	1.9	25.	.45	4.7	46.
49	.18	1.9	25.	.46	4.7	46.
50	.17	1.8	24.	.47	4.8	46.

Table PC-9-B (Continued). Lung Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad, for Nonsmokers. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
51	.17	1.8	24.	.48	4.9	47.
52	.17	1.8	24.	.48	5.0	47.
53	.17	1.8	24.	.49	5.1	48.
54	.17	1.8	24.	.51	5.2	49.
55	.17	1.8	24.	.52	5.3	49.
56	.17	1.8	24.	.54	5.5	50.
57	.17	1.8	24.	.55	5.6	50.
58	.17	1.9	24.	.57	5.8	51.
59	.18	1.9	25.	.58	5.9	52.
60	.18	1.9	25.	.60	6.1	53.
61	.18	1.9	25.	.62	6.3	53.
62	.18	2.0	25.	.64	6.5	54.
63	.19	2.0	26.	.66	6.7	55.
64	.19	2.0	26.	.68	6.9	56.
65	.20	2.1	27.	.70	7.1	57.
66	.20	2.1	27.	.72	7.3	57.
67	.21	2.2	28.	.75	7.5	58.
68	.22	2.3	29.	.78	7.8	59.
69	.23	2.4	30.	.81	8.1	60.
70	.24	2.5	30.	.83	8.3	61.
71	.24	2.6	31.	.85	8.5	61.
72	.25	2.7	32.	.87	8.7	62.
73	.26	2.8	33.	.89	8.8	62.
74	.27	2.9	34.	.90	8.9	63.
75	.28	3.0	34.	.91	9.0	63.

Table PC-9-C. Lung Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad, for Former Smokers.[1] PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose			Dose		
	1	10	100	1	10	100
10	.66	6.7	55.	.65	6.6	55.
11	.60	6.1	53.	.60	6.1	53.
12	.53	5.5	50.	.55	5.6	50.
13	.47	4.9	47.	.50	5.1	48.
14	.42	4.3	44.	.45	4.6	45.
15	.37	3.8	41.	.41	4.2	43.
16	.33	3.4	38.	.37	3.9	41.
17	.29	3.0	35.	.34	3.6	39.
18	.26	2.7	32.	.32	3.3	37.
19	.23	2.5	30.	.29	3.1	35.
20	.21	2.2	28.	.27	2.8	33.
21	.19	2.0	26.	.25	2.6	32.
22	.17	1.8	24.	.23	2.5	30.
23	.16	1.7	23.	.22	2.3	29.
24	.15	1.6	21.	.20	2.2	27.
25	.13	1.4	20.	.19	2.0	26.
26	.12	1.3	19.	.18	1.9	25.
27	.11	1.2	18.	.17	1.8	24.
28	.11	1.1	16.	.16	1.7	23.
29	.099	1.1	15.	.15	1.6	22.
30	.093	.99	15.	.15	1.6	21.
31	.087	.93	14.	.14	1.5	21.
32	.081	.87	13.	.14	1.4	20.
33	.077	.82	12.	.13	1.4	19.
34	.072	.77	12.	.13	1.3	19.
35	.068	.73	11.	.12	1.3	18.
36	.065	.70	11.	.12	1.3	18.
37	.062	.66	10.	.12	1.3	18.
38	.059	.63	9.9	.12	1.2	18.
39	.057	.61	9.5	.11	1.2	17.
40	.055	.59	9.2	.11	1.2	17.
41	.053	.57	8.9	.11	1.2	17.
42	.051	.55	8.6	.11	1.2	17.
43	.050	.53	8.4	.11	1.2	17.
44	.048	.52	8.2	.11	1.2	17.
45	.047	.51	8.0	.11	1.2	17.
46	.046	.50	7.9	.11	1.2	17.
47	.045	.49	7.7	.11	1.2	17.
48	.045	.48	7.6	.11	1.2	17.
49	.044	.47	7.5	.12	1.2	18.
50	.044	.47	7.5	.12	1.3	18.

Table PC-9-C (Continued). Lung Cancer 10 or More Years After
Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex,
and Dose in Rad, for Former Smokers. PC in Percent, to Two
Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
51	.043	.47	7.4	.12	1.3	18.
52	.043	.46	7.4	.12	1.3	18.
53	.043	.46	7.4	.12	1.3	19.
54	.043	.46	7.4	.13	1.4	19.
55	.043	.46	7.4	.13	1.4	20.
56	.043	.47	7.4	.14	1.4	20.
57	.044	.47	7.5	.14	1.5	20.
58	.044	.47	7.5	.14	1.5	21.
59	.044	.48	7.6	.15	1.6	21.
60	.045	.48	7.7	.15	1.6	22.
61	.046	.49	7.8	.16	1.7	22.
62	.046	.50	7.9	.16	1.7	23.
63	.047	.51	8.0	.17	1.8	24.
64	.048	.52	8.2	.17	1.8	24.
65	.050	.53	8.4	.18	1.9	25.
66	.051	.55	8.6	.18	1.9	25.
67	.053	.57	8.9	.19	2.0	26.
68	.055	.59	9.2	.20	2.1	27.
69	.057	.61	9.5	.20	2.2	27.
70	.059	.63	9.9	.21	2.2	28.
71	.062	.66	10.	.22	2.3	29.
72	.064	.68	11.	.22	2.3	29.
73	.066	.71	11.	.22	2.4	29.
74	.069	.73	11.	.23	2.4	30.
75	.071	.76	12.	.23	2.4	30.

Table PC-9-D. Lung Cancer 10 or More Years After Exposure to
Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose
in Rad, for Present Cigarette Smokers, All. PC in Percent,
to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose			Dose		
	1	10	100	1	10	100
10	.24	2.5	30.	.23	2.4	30.
11	.21	2.2	28.	.21	2.2	28.
12	.19	2.0	26.	.19	2.0	26.
13	.17	1.8	24.	.18	1.9	24.
14	.15	1.6	21.	.16	1.7	23.
15	.13	1.4	19.	.14	1.5	21.
16	.12	1.2	18.	.13	1.4	20.
17	.10	1.1	16.	.12	1.3	18.
18	.092	.98	15.	.11	1.2	17.
19	.083	.88	13.	.10	1.1	16.
20	.074	.79	12.	.095	1.0	15.
21	.068	.72	11.	.089	.95	14.
22	.061	.66	10.	.083	.88	13.
23	.056	.60	9.4	.077	.83	12.
24	.052	.55	8.7	.072	.77	12.
25	.048	.51	8.1	.068	.72	11.
26	.044	.47	7.5	.064	.68	11.
27	.041	.44	7.0	.060	.64	10.
28	.038	.40	6.5	.057	.61	9.6
29	.035	.38	6.1	.054	.58	9.1
30	.033	.35	5.7	.052	.56	8.8
31	.031	.33	5.4	.050	.53	8.4
32	.029	.31	5.0	.048	.51	8.1
33	.027	.29	4.8	.046	.49	7.8
34	.026	.27	4.5	.044	.48	7.6
35	.024	.26	4.3	.043	.46	7.4
36	.023	.25	4.1	.042	.45	7.3
37	.022	.23	3.9	.041	.44	7.1
38	.021	.23	3.7	.041	.44	7.0
39	.020	.22	3.6	.040	.43	6.9
40	.019	.21	3.5	.040	.43	6.8
41	.019	.20	3.3	.039	.42	6.8
42	.018	.19	3.2	.039	.42	6.8
43	.018	.19	3.1	.039	.42	6.7
44	.017	.18	3.1	.039	.42	6.7
45	.017	.18	3.0	.039	.42	6.8
46	.016	.18	2.9	.039	.42	6.8
47	.016	.17	2.9	.040	.43	6.9
48	.016	.17	2.8	.040	.43	6.9
49	.016	.17	2.8	.041	.44	7.0
50	.015	.17	2.8	.042	.45	7.1

Table PC-9-D (Continued). Lung Cancer 10 or More Years After
Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex,
and Dose in Rad, for Present Cigarette Smokers, All. PC in
Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose			Dose		
	1	10	100	1	10	100
51	.015	.17	2.8	.042	.45	7.3
52	.015	.16	2.7	.043	.46	7.4
53	.015	.16	2.7	.044	.47	7.5
54	.015	.16	2.7	.045	.49	7.7
55	.015	.16	2.7	.047	.50	7.9
56	.015	.17	2.8	.048	.51	8.1
57	.015	.17	2.8	.049	.53	8.3
58	.016	.17	2.8	.051	.54	8.6
59	.016	.17	2.8	.052	.56	8.8
60	.016	.17	2.9	.054	.57	9.0
61	.016	.17	2.9	.055	.59	9.3
62	.016	.18	2.9	.057	.61	9.5
63	.017	.18	3.0	.059	.63	9.8
64	.017	.18	3.1	.061	.65	10.
65	.018	.19	3.1	.063	.67	10.
66	.018	.19	3.2	.065	.69	11.
67	.019	.20	3.3	.067	.72	11.
68	.019	.21	3.5	.070	.75	11.
69	.020	.22	3.6	.072	.77	12.
70	.021	.23	3.7	.074	.79	12.
71	.022	.23	3.9	.076	.82	12.
72	.023	.24	4.0	.078	.83	13.
73	.023	.25	4.1	.079	.85	13.
74	.024	.26	4.3	.081	.86	13.
75	.025	.27	4.4	.082	.87	13.

Table PC-9-E. Lung Cancer 10 or More Years After Exposure to
Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose
in Rad, for Present Cigarette Smokers, Under 10 per Day.
PC in Percent, to Two Significant Digits or Three Decimal
Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
10	.68	6.9	56.	.66	6.7	55.
11	.61	6.2	53.	.61	6.2	53.
12	.55	5.6	50.	.56	5.7	51.
13	.48	5.0	47.	.50	5.2	48.
14	.43	4.4	44.	.46	4.7	46.
15	.38	3.9	41.	.42	4.3	44.
16	.33	3.5	38.	.38	3.9	41.
17	.30	3.1	36.	.35	3.6	39.
18	.27	2.8	33.	.32	3.4	37.
19	.24	2.5	31.	.30	3.1	35.
20	.21	2.3	28.	.28	2.9	34.
21	.20	2.1	27.	.26	2.7	32.
22	.18	1.9	25.	.24	2.5	31.
23	.16	1.7	23.	.22	2.3	29.
24	.15	1.6	22.	.21	2.2	28.
25	.14	1.5	20.	.20	2.1	27.
26	.13	1.4	19.	.18	2.0	25.
27	.12	1.3	18.	.17	1.8	24.
28	.11	1.2	17.	.17	1.8	23.
29	.10	1.1	16.	.16	1.7	22.
30	.095	1.0	15.	.15	1.6	22.
31	.089	.95	14.	.14	1.5	21.
32	.083	.89	13.	.14	1.5	20.
33	.078	.84	13.	.13	1.4	20.
34	.074	.79	12.	.13	1.4	19.
35	.070	.75	11.	.12	1.3	19.
36	.066	.71	11.	.12	1.3	18.
37	.063	.68	10.	.12	1.3	18.
38	.061	.65	10.	.12	1.3	18.
39	.058	.62	9.7	.12	1.2	18.
40	.056	.60	9.4	.11	1.2	17.
41	.054	.58	9.1	.11	1.2	17.
42	.052	.56	8.8	.11	1.2	17.
43	.051	.54	8.6	.11	1.2	17.
44	.049	.53	8.4	.11	1.2	17.
45	.048	.52	8.2	.11	1.2	17.
46	.047	.51	8.0	.11	1.2	17.
47	.046	.50	7.9	.11	1.2	18.
48	.046	.49	7.8	.12	1.2	18.
49	.045	.48	7.7	.12	1.3	18.

Table PC-9-E (Continued). Lung Cancer 10 or More Years After
    Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex,
    and Dose in Rad, for Present Cigarette Smokers, Under 10
    per Day. PC in Percent, to Two Significant Digits or Three
    Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
50	.045	.48	7.6	.12	1.3	18.
51	.044	.48	7.6	.12	1.3	18.
52	.044	.47	7.6	.12	1.3	19.
53	.044	.47	7.5	.13	1.4	19.
54	.044	.47	7.5	.13	1.4	19.
55	.044	.47	7.6	.13	1.4	20.
56	.044	.48	7.6	.14	1.5	20.
57	.045	.48	7.6	.14	1.5	21.
58	.045	.48	7.7	.15	1.6	21.
59	.046	.49	7.8	.15	1.6	22.
60	.046	.49	7.8	.15	1.6	22.
61	.047	.50	7.9	.16	1.7	23.
62	.047	.51	8.1	.16	1.7	23.
63	.048	.52	8.2	.17	1.8	24.
64	.049	.53	8.4	.17	1.9	24.
65	.051	.54	8.6	.18	1.9	25.
66	.052	.56	8.8	.19	2.0	26.
67	.054	.58	9.1	.19	2.1	26.
68	.056	.60	9.4	.20	2.1	27.
69	.058	.63	9.7	.21	2.2	28.
70	.061	.65	10.	.21	2.3	28.
71	.063	.67	10.	.22	2.3	29.
72	.065	.70	11.	.23	2.4	29.
73	.068	.72	11.	.23	2.4	30.
74	.070	.75	11.	.23	2.4	30.
75	.072	.78	12.	.24	2.5	30.

Table PC-9-F. Lung Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad, for Present Cigarette Smokers, 10 to 20 per Day. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
10	.28	2.9	34.	.27	2.8	33.
11	.25	2.6	31.	.25	2.6	31.
12	.22	2.3	29.	.23	2.4	29.
13	.20	2.1	27.	.20	2.2	27.
14	.17	1.8	24.	.19	2.0	26.
15	.15	1.6	22.	.17	1.8	24.
16	.14	1.4	20.	.15	1.6	22.
17	.12	1.3	18.	.14	1.5	21.
18	.11	1.1	17.	.13	1.4	19.
19	.097	1.0	15.	.12	1.3	18.
20	.087	.93	14.	.11	1.2	17.
21	.079	.85	13.	.10	1.1	16.
22	.072	.77	12.	.097	1.0	15.
23	.066	.71	11.	.090	.96	14.
24	.061	.65	10.	.085	.90	14.
25	.056	.60	9.3	.079	.85	13.
26	.051	.55	8.7	.075	.80	12.
27	.048	.51	8.1	.070	.75	12.
28	.044	.47	7.5	.067	.72	11.
29	.041	.44	7.0	.064	.68	11.
30	.038	.41	6.6	.061	.65	10.
31	.036	.38	6.2	.058	.62	9.7
32	.034	.36	5.9	.056	.60	9.4
33	.032	.34	5.5	.054	.58	9.1
34	.030	.32	5.2	.052	.56	8.8
35	.028	.30	5.0	.051	.54	8.5
36	.027	.29	4.7	.050	.53	8.4
37	.026	.27	4.5	.048	.52	8.2
38	.025	.26	4.3	.048	.51	8.1
39	.024	.25	4.2	.047	.50	8.0
40	.023	.24	4.0	.047	.50	7.9
41	.022	.24	3.9	.046	.49	7.9
42	.021	.23	3.8	.046	.49	7.8
43	.021	.22	3.7	.046	.49	7.8
44	.020	.21	3.6	.046	.49	7.8
45	.020	.21	3.5	.046	.49	7.8
46	.019	.21	3.4	.046	.49	7.9
47	.019	.20	3.3	.047	.50	7.9
48	.019	.20	3.3	.047	.51	8.0
49	.018	.20	3.3	.048	.51	8.1

Table PC-9-F (Continued). Lung Cancer 10 or More Years After
    Exposure to Low-LET Radiation, by Age A₁ at Exposure, Sex,
    and Dose in Rad, for Present Cigarette Smokers, 10 to 20
    per Day. PC in Percent, to Two Significant Digits or Three
    Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
50	.018	.19	3.2	.049	.52	8.2
51	.018	.19	3.2	.050	.53	8.4
52	.018	.19	3.2	.051	.54	8.5
53	.018	.19	3.2	.052	.55	8.7
54	.018	.19	3.2	.053	.57	8.9
55	.018	.19	3.2	.054	.58	9.1
56	.018	.19	3.2	.056	.60	9.4
57	.018	.19	3.2	.057	.61	9.6
58	.018	.20	3.2	.059	.63	9.9
59	.018	.20	3.3	.061	.65	10.
60	.019	.20	3.3	.063	.67	10.
61	.019	.20	3.4	.065	.69	11.
62	.019	.21	3.4	.067	.71	11.
63	.020	.21	3.5	.069	.74	11.
64	.020	.21	3.6	.071	.76	12.
65	.021	.22	3.7	.073	.78	12.
66	.021	.23	3.8	.076	.81	12.
67	.022	.24	3.9	.079	.84	13.
68	.023	.24	4.0	.082	.87	13.
69	.024	.25	4.2	.085	.90	14.
70	.025	.26	4.3	.087	.93	14.
71	.025	.27	4.5	.089	.95	14.
72	.026	.28	4.6	.091	.97	14.
73	.027	.29	4.8	.093	.99	15.
74	.028	.30	5.0	.094	1.0	15.
75	.029	.31	5.1	.096	1.0	15.

Table PC-9-G. Lung Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A, at Exposure, Sex, and Dose in Rad, for Present Cigarette Smokers, 21 to 39 per Day. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
10	.16	1.7	23.	.16	1.7	22.
11	.14	1.5	21.	.14	1.5	21.
12	.13	1.4	19.	.13	1.4	19.
13	.11	1.2	17.	.12	1.3	18.
14	.10	1.1	16.	.11	1.1	17.
15	.088	.94	14.	.098	1.0	15.
16	.078	.83	13.	.089	.95	14.
17	.069	.74	11.	.082	.87	13.
18	.062	.66	10.	.075	.81	12.
19	.056	.60	9.4	.069	.74	11.
20	.050	.54	8.5	.064	.69	11.
21	.046	.49	7.8	.060	.64	10.
22	.042	.45	7.1	.056	.60	9.3
23	.038	.41	6.6	.052	.56	8.8
24	.035	.37	6.1	.049	.52	8.3
25	.032	.34	5.6	.046	.49	7.8
26	.030	.32	5.2	.043	.46	7.4
27	.027	.29	4.8	.041	.44	7.0
28	.025	.27	4.5	.039	.41	6.7
29	.024	.25	4.2	.037	.39	6.4
30	.022	.24	3.9	.035	.38	6.1
31	.021	.22	3.7	.034	.36	5.8
32	.019	.21	3.5	.032	.35	5.6
33	.018	.20	3.3	.031	.33	5.4
34	.017	.19	3.1	.030	.32	5.2
35	.016	.18	2.9	.029	.31	5.1
36	.016	.17	2.8	.029	.31	5.0
37	.015	.16	2.7	.028	.30	4.9
38	.014	.15	2.5	.027	.30	4.8
39	.014	.15	2.4	.027	.29	4.8
40	.013	.14	2.4	.027	.29	4.7
41	.013	.14	2.3	.027	.29	4.7
42	.012	.13	2.2	.026	.28	4.7
43	.012	.13	2.1	.026	.28	4.6
44	.012	.12	2.1	.026	.28	4.6
45	.011	.12	2.0	.026	.28	4.7
46	.011	.12	2.0	.027	.29	4.7
47	.011	.12	2.0	.027	.29	4.7
48	.011	.12	1.9	.027	.29	4.8
49	.011	.11	1.9	.028	.30	4.9

Table PC-9-G (Continued). Lung Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad, for Present Cigarette Smokers, 21 to 39 per Day. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
50	.010	.11	1.9	.028	.30	4.9
51	.010	.11	1.9	.029	.31	5.0
52	.010	.11	1.9	.029	.31	5.1
53	.010	.11	1.9	.030	.32	5.2
54	.010	.11	1.9	.031	.33	5.3
55	.010	.11	1.9	.031	.34	5.5
56	.010	.11	1.9	.032	.35	5.6
57	.010	.11	1.9	.033	.36	5.8
58	.010	.11	1.9	.034	.37	5.9
59	.011	.11	1.9	.035	.38	6.1
60	.011	.12	1.9	.036	.39	6.3
61	.011	.12	2.0	.037	.40	6.4
62	.011	.12	2.0	.038	.41	6.6
63	.011	.12	2.0	.040	.43	6.8
64	.012	.12	2.1	.041	.44	7.0
65	.012	.13	2.1	.042	.45	7.2
66	.012	.13	2.2	.044	.47	7.5
67	.013	.14	2.3	.045	.49	7.7
68	.013	.14	2.4	.047	.50	8.0
69	.014	.15	2.5	.049	.52	8.3
70	.014	.15	2.5	.050	.54	8.5
71	.015	.16	2.6	.052	.55	8.7
72	.015	.16	2.7	.053	.56	8.9
73	.016	.17	2.8	.054	.57	9.0
74	.016	.18	2.9	.054	.58	9.1
75	.017	.18	3.0	.055	.59	9.3

Table PC-9-H. Lung Cancer 10 or More Years After Exposure to
Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose
in Rad, for Present Cigarette Smokers, 40 or More per Day.
PC in Percent, to Two Significant Digits or Three Decimal
Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
10	.11	1.2	17.	.11	1.2	17.
11	.10	1.1	16.	.10	1.1	16.
12	.090	.96	14.	.092	.98	15.
13	.080	.85	13.	.083	.89	13.
14	.070	.75	11.	.076	.81	12.
15	.062	.66	10.	.069	.74	11.
16	.055	.59	9.2	.063	.67	10.
17	.049	.52	8.3	.058	.62	9.6
18	.044	.47	7.5	.053	.57	8.9
19	.039	.42	6.8	.049	.53	8.3
20	.035	.38	6.1	.045	.49	7.7
21	.032	.34	5.6	.042	.45	7.2
22	.029	.31	5.1	.039	.42	6.8
23	.027	.29	4.7	.037	.39	6.4
24	.025	.26	4.3	.034	.37	6.0
25	.023	.24	4.0	.032	.35	5.6
26	.021	.22	3.7	.030	.33	5.3
27	.019	.21	3.4	.029	.31	5.0
28	.018	.19	3.2	.027	.29	4.8
29	.017	.18	3.0	.026	.28	4.6
30	.016	.17	2.8	.025	.27	4.4
31	.015	.16	2.6	.024	.25	4.2
32	.014	.15	2.5	.023	.24	4.0
33	.013	.14	2.3	.022	.24	3.9
34	.012	.13	2.2	.021	.23	3.8
35	.011	.12	2.1	.021	.22	3.7
36	.011	.12	2.0	.020	.22	3.6
37	.010	.11	1.9	.020	.21	3.5
38	.010	.11	1.8	.019	.21	3.5
39	.010	.10	1.7	.019	.21	3.4
40	.009	.099	1.7	.019	.20	3.4
41	.009	.096	1.6	.019	.20	3.4
42	.009	.093	1.6	.019	.20	3.3
43	.008	.090	1.5	.019	.20	3.3
44	.008	.087	1.5	.019	.20	3.3
45	.008	.085	1.4	.019	.20	3.3
46	.008	.083	1.4	.019	.20	3.4
47	.008	.082	1.4	.019	.20	3.4
48	.008	.081	1.4	.019	.21	3.4
49	.007	.080	1.3	.019	.21	3.5

Table PC-9-H (Continued). Lung Cancer 10 or More Years After
Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex,
and Dose in Rad, for Present Cigarette Smokers, 40 or More
per Day. PC in Percent, to Two Significant Digits or Three
Decimal Places.

A_1	Sex					
	Male			Female		
	Dose			Dose		
	1	10	100	1	10	100
50	.007	.079	1.3	.020	.21	3.5
51	.007	.078	1.3	.020	.22	3.6
52	.007	.078	1.3	.021	.22	3.7
53	.007	.078	1.3	.021	.23	3.7
54	.007	.078	1.3	.022	.23	3.8
55	.007	.078	1.3	.022	.24	3.9
56	.007	.078	1.3	.023	.24	4.0
57	.007	.079	1.3	.023	.25	4.1
58	.007	.079	1.3	.024	.26	4.3
59	.008	.080	1.4	.025	.27	4.4
60	.008	.081	1.4	.025	.27	4.5
61	.008	.083	1.4	.026	.28	4.6
62	.008	.084	1.4	.027	.29	4.8
63	.008	.085	1.4	.028	.30	4.9
64	.008	.087	1.5	.029	.31	5.1
65	.008	.090	1.5	.030	.32	5.2
66	.009	.093	1.6	.031	.33	5.4
67	.009	.096	1.6	.032	.34	5.6
68	.009	.099	1.7	.033	.36	5.8
69	.010	.10	1.7	.034	.37	6.0
70	.010	.11	1.8	.035	.38	6.1
71	.010	.11	1.9	.036	.39	6.3
72	.011	.12	1.9	.037	.40	6.4
73	.011	.12	2.0	.038	.40	6.5
74	.012	.12	2.1	.038	.41	6.6
75	.012	.13	2.1	.039	.42	6.7

Table PC-9-I.   Lung Cancer, by Cumulative Exposure to Radon Daughters, in WLM, and by Assumed Risk Factor, for Exposure 10 or More Years Before Diagnosis.   PC in Percent.

WLM	Assumed Percent Excess Risk per WLM		
	0.7	1.2	1.5
1	0.7	1.2	1.5
2	1.4	2.3	2.9
3	2.1	3.5	4.3
4	2.7	4.6	5.7
5	3.4	5.7	7.0
6	4.0	6.7	8.3
7	4.7	7.7	9.5
8	5.3	8.8	11.
9	5.9	9.7	12.
10	6.5	11.	13.
11	7.1	12.	14.
12	7.7	13.	15.
13	8.3	13.	16.
14	8.9	14.	17.
15	9.5	15.	18.
16	10.	16.	19.
17	11.	17.	20.
18	11.	18.	21.
19	12.	19.	22.
20	12.	19.	23.
25	15.	23.	27.
30	17.	26.	31.
35	20.	30.	34.
40	22.	32.	38.
45	24.	35.	40.
50	26.	38.	43.
60	30.	42.	47.
70	33.	46.	51.
80	36.	49.	55.
90	39.	52.	57.
100	41.	55.	60.
120	46.	59.	64.
140	49.	63.	68.
160	53.	66.	71.
180	56.	68.	73.
200	58.	71.	75.
250	64.	75.	79.
300	68.	78.	82.
350	71.	81.	84.
400	74.	83.	86.
450	76.	84.	87.
500	78.	86.	88.
600	81.	88.	90.
700	83.	89.	91.
800	85.	91.	92.
900	86.	92.	93.
1000	88.	92.	94.

Table PC-10. Female Breast Cancer 10 or More Years After
   Exposure to Low-LET Radiation, by Age A_1 at Exposure and
   Dose in Rad. PC in Percent, to Two Significant Digits or
   Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose			Dose		
	1	10	100	1	10	100
0	---	---	---	2.3	19.	70.
1	---	---	---	2.3	19.	70.
2	---	---	---	2.2	19.	70.
3	---	---	---	2.2	18.	69.
4	---	---	---	2.0	17.	68.
5	---	---	---	1.9	17.	66.
6	---	---	---	1.8	16.	65.
7	---	---	---	1.7	15.	64.
8	---	---	---	1.6	14.	62.
9	---	---	---	1.5	13.	60.
10	---	---	---	1.4	13.	59.
11	---	---	---	1.3	12.	57.
12	---	---	---	1.2	11.	56.
13	---	---	---	1.2	11.	54.
14	---	---	---	1.1	10.	53.
15	---	---	---	1.1	9.7	52.
16	---	---	---	.98	9.0	50.
17	---	---	---	.89	8.2	47.
18	---	---	---	.79	7.4	44.
19	---	---	---	.69	6.5	41.
20	---	---	---	.60	5.7	38.
21	---	---	---	.52	5.0	34.
22	---	---	---	.45	4.3	31.
23	---	---	---	.39	3.8	28.
24	---	---	---	.35	3.4	26.
25	---	---	---	.33	3.2	25.
26	---	---	---	.31	3.0	24.
27	---	---	---	.30	2.9	23.
28	---	---	---	.28	2.8	22.
29	---	---	---	.28	2.7	22.
30	---	---	---	.27	2.6	21.
31	---	---	---	.26	2.5	21.
32	---	---	---	.25	2.4	20.
33	---	---	---	.24	2.4	19.
34	---	---	---	.23	2.2	19.
35	---	---	---	.21	2.1	18.
36	---	---	---	.19	1.9	16.
37	---	---	---	.17	1.7	15.
38	---	---	---	.15	1.5	13.
39	---	---	---	.13	1.2	11.
40	---	---	---	.10	1.0	9.4

Table PC-10 (Continued). Female Breast Cancer 10 or More Years
    After Exposure to Low-LET Radiation, by Age A_1 at Exposure
    and Dose in Rad. PC in Percent, to Two Significant Digits
    or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
41	---	---	---	.083	.83	7.7
42	---	---	---	.067	.66	6.3
43	---	---	---	.055	.54	5.2
44	---	---	---	.048	.48	4.6
45	---	---	---	.045	.45	4.3
46	---	---	---	.043	.43	4.1
47	---	---	---	.041	.41	3.9
48	---	---	---	.039	.39	3.8
49	---	---	---	.037	.37	3.6
50	---	---	---	.036	.36	3.5
51	---	---	---	.034	.34	3.3
52	---	---	---	.033	.33	3.2
53	---	---	---	.032	.32	3.1
54	---	---	---	.030	.30	3.0
55	---	---	---	.029	.29	2.8
56	---	---	---	.028	.28	2.7
57	---	---	---	.026	.26	2.6
58	---	---	---	.025	.25	2.4
59	---	---	---	.023	.23	2.3
60	---	---	---	.021	.21	2.1
61	---	---	---	.020	.20	2.0
62	---	---	---	.018	.18	1.8
63	---	---	---	.017	.17	1.7
64	---	---	---	.015	.15	1.5
65	---	---	---	.014	.14	1.4
66	---	---	---	.013	.13	1.3
67	---	---	---	.011	.11	1.1
68	---	---	---	.010	.10	.99
69	---	---	---	.008	.086	.85
70	---	---	---	.007	.072	.71
71	---	---	---	.005	.058	.58
72	---	---	---	.004	.044	.44
73	---	---	---	.002	.029	.29
74	---	---	---	.001	.015	.15
75	---	---	---	.000	.000	.000

Table PC-11. Kidney and Bladder Cancer 10 or More Years After
Exposure to Low-LET Radiation, by Age A_1 at Exposure,
Sex, and Dose in Rad. PC in Percent, to Two Significant
Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
20	.12	1.3	19.	.30	3.2	36.
21	.12	1.2	18.	.29	3.0	35.
22	.11	1.2	17.	.27	2.9	34.
23	.10	1.1	16.	.26	2.7	33.
24	.095	1.0	15.	.25	2.6	32.
25	.089	.95	14.	.24	2.5	30.
26	.083	.89	13.	.22	2.4	29.
27	.078	.83	13.	.21	2.2	28.
28	.073	.78	12.	.20	2.1	27.
29	.069	.73	11.	.19	2.0	26.
30	.065	.69	11.	.18	1.9	25.
31	.061	.66	10.	.17	1.8	24.
32	.058	.62	9.7	.16	1.7	23.
33	.055	.59	9.2	.16	1.7	23.
34	.052	.56	8.8	.15	1.6	22.
35	.050	.53	8.4	.14	1.5	21.
36	.048	.51	8.1	.14	1.5	20.
37	.045	.49	7.7	.13	1.4	19.
38	.043	.47	7.4	.13	1.3	19.
39	.042	.45	7.1	.12	1.3	18.
40	.040	.43	6.9	.12	1.3	18.
41	.038	.41	6.6	.11	1.2	17.
42	.037	.40	6.4	.11	1.2	17.
43	.036	.38	6.2	.11	1.1	17.
44	.034	.37	6.0	.10	1.1	16.
45	.033	.36	5.8	.10	1.1	16.
46	.032	.35	5.7	.10	1.1	16.
47	.032	.34	5.5	.098	1.0	15.
48	.031	.33	5.4	.097	1.0	15.
49	.030	.32	5.3	.095	1.0	15.
50	.030	.32	5.2	.094	1.0	15.
51	.029	.31	5.1	.093	.99	15.
52	.029	.31	5.0	.092	.98	15.
53	.028	.30	5.0	.091	.97	14.
54	.028	.30	4.9	.090	.97	14.
55	.028	.30	4.9	.090	.96	14.
56	.028	.30	4.8	.090	.96	14.
57	.027	.29	4.8	.090	.96	14.
58	.027	.29	4.8	.090	.96	14.
59	.027	.29	4.8	.090	.96	14.
60	.027	.29	4.8	.090	.96	14.

Table PC-11 (Continued). Kidney and Bladder Cancer 10 or
More Years After Exposure to Low-LET Radiation, by Age A_1
at Exposure, Sex, and Dose in Rad. PC in Percent, to Two
Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
61	.027	.29	4.8	.090	.96	14.
62	.027	.29	4.8	.090	.97	14.
63	.027	.29	4.8	.091	.97	14.
64	.027	.29	4.8	.091	.97	14.
65	.027	.29	4.8	.091	.98	14.
66	.028	.30	4.9	.092	.98	15.
67	.028	.30	4.9	.093	.99	15.
68	.028	.30	4.9	.093	.99	15.
69	.029	.31	5.0	.094	1.0	15.
70	.029	.31	5.1	.095	1.0	15.
71	.029	.31	5.1	.096	1.0	15.
72	.030	.32	5.2	.097	1.0	15.
73	.030	.32	5.3	.098	1.0	15.
74	.031	.33	5.3	.099	1.1	15.
75	.031	.33	5.4	.10	1.1	16.

Table PC-12. Thyroid Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
0	9.6	51.	91.	9.1	50.	91.
1	8.8	49.	91.	8.5	48.	90.
2	8.1	47.	90.	8.0	47.	90.
3	7.6	45.	89.	7.6	45.	89.
4	7.1	43.	88.	7.2	44.	89.
5	6.7	42.	88.	6.8	42.	88.
6	6.3	40.	87.	6.5	41.	88.
7	6.0	39.	86.	6.3	40.	87.
8	5.7	38.	86.	6.0	39.	86.
9	5.4	36.	85.	5.8	38.	86.
10	5.2	35.	85.	5.6	37.	86.
11	5.0	34.	84.	5.5	37.	85.
12	4.8	34.	83.	5.3	36.	85.
13	4.6	33.	83.	5.2	36.	85.
14	4.5	32.	82.	5.2	35.	84.
15	4.4	31.	82.	5.1	35.	84.
16	4.1	30.	81.	4.9	34.	84.
17	3.8	28.	80.	4.7	33.	83.
18	3.5	26.	78.	4.4	31.	82.
19	3.1	24.	76.	4.0	29.	81.
20	2.7	22.	74.	3.6	27.	79.
21	2.4	20.	71.	3.2	25.	77.
22	2.1	18.	68.	2.8	22.	74.
23	1.8	16.	65.	2.4	20.	71.
24	1.6	14.	61.	2.1	18.	68.
25	1.4	12.	58.	1.8	16.	65.
26	1.3	11.	56.	1.7	15.	63.
27	1.2	11.	55.	1.6	14.	62.
28	1.2	11.	55.	1.6	14.	63.
29	1.2	11.	55.	1.7	14.	63.
30	1.2	11.	54.	1.7	14.	63.
31	1.2	11.	54.	1.7	15.	63.
32	1.1	10.	54.	1.7	15.	63.
33	1.1	10.	53.	1.7	15.	63.
34	1.1	10.	53.	1.7	15.	64.
35	1.1	9.9	52.	1.7	15.	64.
36	1.1	9.7	52.	1.7	15.	64.
37	1.0	9.6	51.	1.7	15.	64.
38	1.0	9.4	51.	1.7	15.	64.
39	1.0	9.3	50.	1.7	15.	64.
40	1.0	9.2	50.	1.7	15.	64.

Table PC-12 (Continued). Thyroid Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
41	.98	9.0	50.	1.7	15.	64.
42	.97	8.9	50.	1.7	15.	64.
43	.96	8.9	49.	1.7	15.	64.
44	.95	8.8	49.	1.7	15.	64.
45	.94	8.7	49.	1.7	15.	64.
46	.93	8.6	48.	1.7	15.	64.
47	.91	8.4	48.	1.7	15.	64.
48	.89	8.3	47.	1.7	15.	63.
49	.88	8.1	47.	1.7	15.	63.
50	.86	8.0	46.	1.7	15.	63.
51	.84	7.8	46.	1.7	15.	63.
52	.82	7.7	45.	1.7	15.	63.
53	.81	7.5	45.	1.7	14.	63.
54	.79	7.4	44.	1.6	14.	63.
55	.78	7.3	44.	1.6	14.	62.
56	.77	7.2	44.	1.6	14.	62.
57	.76	7.1	43.	1.6	14.	62.
58	.76	7.1	43.	1.6	14.	62.
59	.75	7.0	43.	1.6	14.	62.
60	.75	7.0	43.	1.6	14.	62.
61	.74	7.0	43.	1.6	14.	62.
62	.74	6.9	43.	1.6	14.	62.
63	.73	6.9	42.	1.6	14.	62.
64	.73	6.8	42.	1.6	14.	62.
65	.72	6.8	42.	1.6	14.	62.
66	.72	6.7	42.	1.6	14.	62.
67	.71	6.7	42.	1.6	14.	62.
68	.71	6.7	42.	1.6	14.	63.
69	.71	6.6	42.	1.7	14.	63.
70	.71	6.7	42.	1.7	14.	63.
71	.71	6.7	42.	1.7	14.	63.
72	.72	6.8	42.	1.6	14.	63.
73	.74	6.9	43.	1.6	14.	63.
74	.76	7.1	43.	1.6	14.	62.
75	.78	7.3	44.	1.6	14.	62.

APPENDIX II - STATUS OF FINAL REPORT OF THE WORKING GROUP IN RELATION

TO THE RECOMMENDATIONS OF THE NATIONAL ACADEMY OF SCIENCES (NAS)

OVERSIGHT COMMITTEE ON AN EARLIER DRAFT (JULY, 1984)

     The NIH Working Group has been in close communication with the NAS Oversight Committee throughout the period during which the Radioepidemiological Tables have been in preparation. In consequence, many of the recommendations made by the Oversight Committee on the July draft have been followed in the preparation of the final draft. Others, of course, look to the future and counsel any future group that may have the task of preparing revisions. In what follows, the NAS recommendations are first reproduced individually and a statement is provided to show how that topic has been handled in the final report.

1.   "The Oversight Committee recommends that the Working Group prominently indicate that the doses used in the tables are absorbed doses in organs and that use of other radiation measures, such as kerma or instrument readings, in calculating assigned shares will results in errors."

     The final report should make it clear that the dose to be used for each site is the absorbed dose. Chapters IV, V, VI, and IX, in which the methodology is outlined, all refer to dose as "absorbed", "tissue", or "organ" dose, and in Chapter X the PC calculation for each site is given in terms of absorbed dose.

2.   "The Oversight Committee recommends that the Working Group consider other ways of defining the category of "leukemia excluding CLL" (chronic lymphocytic leukemia)-- for example, ways that would exclude cases that should be diagnosed as CLL but are not."

     The Working Group's definition of a disease that included all types of leukemia other than chronic lymphocytic leukemia (CLL) was based on the previous use of this definition by the BEIR III Committee and on the fact that CLL is the only major type of leukemia that has not been observed to increase in incidence in irradiated human populations. It is true, as stated by the Oversight Committee, that this definition can result in the inclusion of cases of CLL that are not diagnosed as such. However, no classification can protect entirely against misdiagnosis. To define the category by inclusion rather than exclusion based on current diagnostic criteria would require re-analysis of all the leukemia case material from the A-bomb survivors, ankylosing spondylitics, Thorotrast patients and other series, which is probably not feasible.

3.   "The Oversight Committee recommends that the decision of whether to include specific sites of cancer in the radioepidemiologic tables be based, to the extent possible, on an evaluation of the reliability of the estimates of assigned share, rather than on a subjective judgment preceding the data analysis."

It may well be that all tissues in which cancers arise are sus-
ceptible to the carcinogenic effect of ionizing radiation, but this
has not been shown. The Working Group employed three criteria in
selecting sites:

(1) The available evidence indicates that cancers of
     the site in question may be caused by ionizing
     radiation;

(2) There are risk coefficients of sufficient specificity
     as to age and sex to permit the calculation of PC
     tables; and

(3) The risk coefficients have sufficient stability to
     warrant the calculation of PC estimates.

4.   "The Oversight Committee recommends that, in compiling assigned shares
in the future, greater use be made of original radioepidemiologic data,
including the latest updates available, and that correspondingly less use
be made of derived risk coefficients, such as those from the BEIR III report."

The Working Group agrees that future revisions of the Tables should
include original risk estimates from the latest available data and
notes that a somewhat larger committee operating in a longer time
frame would be desirable. However, care should be taken to avoid
unnecessary duplication between a future committee's work and that
of a new BEIR committee of the NAS.

5.   "The Oversight Committee recommends that the use of mortality data be
considered for improving the understanding of the baseline incidence data
and for identifying the uncertainties in the trends for those data."

The Working Group examined mortality trends over time and in-
cluded in Chapter VII-C remarks concerning the several sites for
which such trends are most important.

6.   "The Oversight Committee recommends that the Working Group explain in
greater detail the consequences of different time-projection models.
Different models not only distribute observed cancer risks differently
over the period of observation, but also lead to different estimates or
risk for longer periods after exposure. The best choice of model is still
uncertain, and the users of the tables should understand their limitations."

The Working Group agrees with the Oversight Committee that the
choice of a time-projection or time-to-tumor model can have
profound implications for PC, or assigned share, calculations.
Many pages of text have been devoted to this topic in Chapters
III, V and VII, in addition to text and tables in the site-specific
sections of Chapter X. Much discussion has been devoted to the
fitting of lognormal time-to-tumor distributions to data for bone
cancer and leukemia, and to the choice of the constant relative
risk model for the other cancer sites treated. The latter choice
was based on the plausibility of the model in the context of a
multi-stage hypothesis for radiation carcinogenesis, in which

radiation acts at an early stage, and on analyses of data for breast, lung, and stomach cancer. For those sites, the constant relative risk model fits well. The extension of the model to other sites receives support from analyses by Kato and Schull (4, Chapter V) showing that the relative risk for all cancers other than leukemia, considered as a group, varies little over time, within age-at-exposure cohorts. Also, Darby's analyses in parallel of mortality data from the A-bomb survivor and British spondylitic series (18, Chapter V) indicates that the model holds for the group of sites heavily irradiated in the latter series. Only for thyroid cancer is there reason to believe that relative risk may vary over time; this variation may, however, merely reflect unusually thorough ascertainment in irradiated populations thought to be at elevated risk.

7. "The Oversight Committee recommends that the Working Group provide explicit guidance on projecting risks beyond the period of observed data—e.g., how to estimate an assigned share for a person whose cancer occurs more than 35 years after exposure—or else provide an explicit statement that it cannot now be done."

> The tables for leukemia and bone cancer have been carried out to 49 years, but for other sites, where the relative risk time distribution model is employed, the tables permit PC's to be estimated for any period following exposure. The user is informed as to the specific period of observation on which the underlying data for other sites are based and alerted to the additional uncertainty attending PC estimates for longer periods.

8. "The Oversight Committee recommends that full consideration be given to the possibility of reanalyzing the available statistics on excess cancer to model their time dependence without any specific assumptions about period of latency, rather than assuming a fixed minimal latent period and a prescribed form for the hazard function."

> (See comment following 9 below.)

9. "The Oversight Committee recommends that, if analyses like those described in Recommendation 8 prove ineffective, consideration be given to allowing different minimal latency periods and different periods during which relative risks increase, for each specific type of cancer and age at exposure."

> Minimal latent period is very difficult to investigate except when the relative excess risk is extremely high, as for bone sarcoma in patients exposed to radium-224. Another complication is that, for example in the case of breast cancer among women exposed at young ages, it would be possible for the true relative risk to be fairly high at ages of very low baseline risk, without any cancers being observed even in a large sample. The approaches recommended by the Oversight Committee are in fact no different from what actually has been

done; the discussion by the Working Group reflects
the fact that these approaches seldom are successful.

10. "The Oversight Committee recommends that the assumption of constant
relative risks be reassessed as new data and new methods of analysis appear."

 This is for the future, but the Working Group endorses the
 recommendation.

11. "The Oversight Committee recommends that the method for projecting
relative risk estimates among populations be reconsidered when the
tables are next revised."

 This is for the future, but the Working Group endorses the
 recommendation.

12. "The Oversight Committee recommends that each revision of the tables
include a fresh appraisal of the relationship between cancer risks and
radiation dose and dose rate, allowing different responses under different
conditions for different tumor types."

 This also is for the future, but scarcity of human data may always
 force reliance on experimental results with animal models.

13. "The Oversight Committee recommends that the Working Group further
justify its decision on how to apply quality factors in calculating
assigned shares for various high-LET radiations."

 (See comment following 14 below.)

14. "The Oversight Committee recommends that a method for estimating
assigned shares for persons exposed to high-LET radiation be developed
that does not depend so heavily on the estimates for low-LET radiation."

 In the final report, the Working Group has abandoned the use of
 quality factors (Q) for estimating the cancer risk from high-LET
 radiation. In the narrowest sense, Q for a given type of radia-
 tion may be viewed as a somewhat arbitrarily selected constant
 "relative biological effectiveness" (RBE) factor. The use of Q
 makes sense from a radiation protection standpoint, in that it
 enables one to express doses of radiation of different qualities
 on a common scale (dose equivalent in rem). In reality, the RBE
 of a given radiation varies with the end point studied, the
 energy (and hence the LET) of the radiation at the target site,
 the total dose and in many cases the dose rate. Therefore, it
 is not possible to assign a single RBE value for a given type of
 high-LET radiation, say, fast neutrons. For internal emitters
 (deposited radionuclides), dosimetry is further complicated by
 variations in spatial and temporal distributions of the radiation
 sources within the target tissues. For these reasons, the
 Working Group has limited its consideration of high-LET radiation
 to cases where data from direct observations exist, i.e., exposures
 of bone to radium-224 (in which case the alpha-radiation dose is
 measured in rad) and exposure of lung to radon daughters (radiation
 exposure in working level months, WLM).

15. "The Oversight Committee recommends that the current assumptions about the relationships between radiation and smoking be reviewed as new information on both low- and high-LET exposures accumulates."

> The human data on the interaction between smoking and radiation leave much to be desired and the Working Group can only endorse this recommendation.

16. "The Oversight Committee recommends that the Working Group provide sufficient further documentation of its approach to handling dose rate for the calculations to be reproduced independently. Graphic displays showing the distribution of dose over time may be useful."

> The handling of dose-rate effect has been discussed in Chapter V, Section B. Specific examples are provided in Chapter IX, Example 5, and in examples for the specific sites in Chapter X.

17. "The Oversight Committee recommends investigation of the possibility of modeling the response to radiation to include a variable for dose rate as well as dose, age at exposure, and age at diagnosis, with a smooth variation in response to changes in any variable."

> The Oversight Committee's recommendation suggests that there is some intrinsic advantage in using smooth models to analyze data as opposed to smoothing estimates derived from partitioned data. This seems debatable in the absence of theoretical models specifying the dependence of risk on various factors used to define the partition. Such models do exist for dose response, and the Working Group's calculations and those of the BEIR Committee incorporate them. Such models do not exist for the effect of age at exposure, on the other hand, and it seems reasonable to base the method of smoothing, if any is to be employed, at least partly on the way in which risk is observed to vary with exposure age.

18. "The Oversight Committee recommends that the Working Group discuss in detail the methods, data, assumptions, and calculations that need to be made to estimate assigned shares for radiation as a cause of cancer. Such a discussion would be useful to the users, as well as in the production of improved versions of the tables."

> The Working Group believes that it has performed this necessary task in a way that will aid in the use as well as the revision of the tables.

19. "The Oversight Committee recommends that, before the Working Group disbands, it document completely the derivation of the factors used in the calculation of an assigned share."

> The Working Group believes that it has provided adequate documentation.

20. "The Oversight Committee recommends that a well-documented set of computer programs be developed to facilitate both tabulation of the

factors used in the formulas and unambiguous application of the assigned-share forumlas."

The Working Group has prepared a documented version of the
programs used in its calculations. There should be little diffi-
culty in adapting these programs, which are written in MLAB, to
other programming languages.

21. "The Oversight Committee recommends that an alternative expression be
considered for 'probability of causation,' such as 'assigned share,' that
more accurately reflects what is being estimated."

The Working Group preferred to use the language of the enabling
Orphan Drug Act.

22. "The Oversight Committee recommends that the possibility of using a
different partition of the populations be kept in mind when new versions
of the tables are being produced, to be consistent with relevant newly
available information."

This recommendation also is for the future and one the Working
Group can endorse.

23. "The Oversight Committee recommends that the available radioepidemiologic
data be analyzed with techniques that exploit the inherent smoothness of
the relevant biologic processes."

See response to recommendation no. 17.

24. "The Oversight Committee recommends that the Working Group conduct a
quantitative appraisal, such as a sensitivity analysis, to evaluate the
uncertainties in the assumptions, data, and methods used in constructing
the tables; their influence on the reliability of the tables of assigned
shares; and their implications for possible uses of the tables."

The Working Group has included a discussion of the elements that
contribute to uncertainty in Chapter VII. A quantitative analysis
of the influence of these elements on the reliability of the
estimates of the tables of Probability of Causation has been
included as Chapter VII, Section O.

25. "The Oversight Committee recommends that the tables of assigned shares
be updated promptly after the revised atomic-bomb dosimetry is released,
with cancer data through 1982 or later if available and analysis with
improved techniques if possible."

In Chapter VIII the Working Group has taken this position.

APPENDIX III - GLOSSARY

Absolute risk -

an expression of excess risk based on the assumption that the excess risk from radiation exposure adds to the underlying (baseline) risk, by a constant increment dependent on dose; an absolute risk time-response model distributes the radiogenic risk after exposure independently of the underlying natural risk.

Additive interaction model (AIM) -

the assumption that the total excess risk from exposures to radiation and to another risk factor is equal to the sum of the excess risks from the two taken separately.

Alpha particle -

a charged particle emitted from certain unstable atomic nuclei (radio-active elements), having the physical characteristics of a helium nucleus (mass 4, charge 2+).

Ankylosing spondylitis -

arthritis of the spine.

Assigned share -

a number that expresses the probability that a given cancer is caused by a previous exposure to a carcinogenic agent, such as radiation; here synonymous with "probability of causation" (PC).

Ataxia telangiectasia (AT)

an inherited disorder associated with an increased risk of cancer, lymphoma in particular, and characterized by immunologic, chromosomal, and DNA defects.

ATB -

at the time of the bomb; referring to the dropping of the atomic bombs at Hiroshima and Nagasaki in 1945.

Background radiation -

the amount of radiation to which a member of the population is exposed from natural sources, such as terrestrial radiation from naturally occurring radionuclides in the soil, cosmic radiation originating in outer space, and naturally occurring radionuclides deposited in the human body. The natural background radiation received by an individual depends on geographic location and living habits. In the U.S., the background radiation is on the order of 100-200 mrem per year.

Baseline rate -

the cancer experience observed in a population in the absence of the
specific agent being studied; the baseline rate might, however, include
cancers from a number of other causes, such as smoking, background
radiation, etc. The Working Group has used data from the SEER program
(see this) as baseline rates for the present report.

BEIR III -

refers to the third National Academy of Sciences' Committee on
Biological Effects of Ionizing Radiation, as well as to the report
published by this committee in 1980; the 1972 BEIR I report was also
used by the Working Group.

Beta particle -

a charged particle emitted from the nucleus of certain unstable atomic
nuclei (radioactive elements), having the charge (+ 1 or -1) and mass of
an electron.

Biologically equivalent dose (BED) -

for a given dose and quality of radiation, and for a given cancer
site, the BED is the dose of 250 kVp X rays required to produce the
same increase in cancer risk.

Cancer -

a malignant tumor of potentially unlimited growth, capable of invading
surrounding tissue or spreading to other parts of the body by metastasis.

Carcinogen -

an agent that may cause cancer. Ionizing radiations are physical
carcinogens; there are also chemical and biologic carcinogens and
biologic carcinogens may be external (e.g., viruses) or internal
(genetic defects).

Carcinoma -

a malignant tumor (cancer) of epithelial origin.

Case-control study -

an epidemiological study in which people with disease are compared with
a similarly composed group of people without disease and the histories
of exposures to a putative causative agent are compared.

Cohort study -

or follow-up study; an epidemiological study in which groups of people
are identified with respect to the presence or absence of exposure to
a disease-causing agent and the outcomes in terms of disease rates are
compared.

Confidence interval -

   an interval estimate of a statistical parameter, obtained as a
   particular function of observed values of one or more random
   variables whose joint distribution depends upon that parameter.
   The interval-valued function is so defined that, in an infinitely
   increasing number of independent replications of the experiment
   yielding the observed values of the random variables, the propor-
   tion of times that the interval contains the (unknown) parameter
   value converges to a number at least as large as some preset value,
   called the confidence level of the interval.

Credibility interval -

   an analogue of confidence interval, in terms of subjective probability.
   If one's information about the true value of an unknown parameter can
   be summarized by a probability distribution for that value, a credi-
   bility interval of a given probability level for the parameter is an
   interval such that the subjective probability distribution, integrated
   over the interval, is not less than the given probability level.

Crossover dose -

   that value of the radiation dose for which the contributions of the linear
   and quadratic components of the linear-quadratic dose-response function
   are equal. A crossover dose of zero corresponds to a pure quadratic
   dose-effect function, and an infinite crossover dose corresponds to a
   pure linear dose-effect function.

DNA -

   deoxyribonucleic acid; the genetic material of cells.

Dose = absorbed radiation dose -

   see: rad.

Dose-effect (dose-response) model -

   a mathematical formulation of the way in which the effect, or
   response, depends on dose.

Dose equivalent -

   a quantity that expresses all radiations on a common scale for cal-
   culating the effective absorbed dose. Dose equivalent is defined as
   the product of the absorbed dose in rad and certain modifying factors
   (the most important being the so-called quality factor, Q) and is expressed
   in units of "rem" (see this).

Dose rate -

   the quantity of absorbed dose delivered per unit time.

Epidemiology –

> the study of the determinants of the frequency of disease in man. The two main types of epidemiological studies of chronic disease are cohort (or follow-up) studies and case-control (or retrospective) studies.

Etiology –

> the science or description of cause(s) of disease.

Fallout –

> radioactive debris from a nuclear detonation or other source, usually deposited from air-borne particulates.

Fluoroscopy –

> a method of visualizing internal structures by directing X rays through an object (e.g., part of the body) onto a fluorescent screen.

Fractionation –

> the delivery of a given total dose of radiation as several smaller doses, separated by intervals of time.

Gamma radiation –

> also gamma rays; short wavelength electromagnetic radiation of nuclear origin, similar to X rays but usually of higher energy (10 keV to 9 MeV).

Geometric mean –

> the geometric mean of a set of positive numbers is the exponential of the arithmetic mean of their logarithms. The geometric mean of a lognormal distribution is the exponential of the mean of the associated normal distribution.

Geometric standard deviation (GSD) –

> the geometric standard deviation of a lognormal distribution is the exponential of the standard deviation of the associated normal distribution. The geometric standard deviation is not standard for statistical terminology but is more commonly used by physicists.

Half-life –

> (physical); the time required for a radioactive element to lose 50% of its activity by decay.

High-LET radiation –

> radiation producing high ionization density along its track; includes neutrons, protons, alpha particles, and the charged nuclei of higher atomic-weight elements (see LET).

ICDA –

>the International Classification of Diseases Adapted for use in the
>U.S. The ICD is periodically revised by the World Health Organization;
>the 8th ICDA is adapted from the 8th ICD and was issued in 1972.

ICRP –

>International Commission on Radiological Protection.

Incidence –

>or incidence rate; the rate of occurrence of a disease within a
>specified period of time, often expressed as number of cases per
>100,000 individuals per year.

In utero –

>in the womb, i.e., before birth.

In vitro –

>(literally, in glass), in culture or in the test-tube (as opposed to
>in vivo, in the living individual).

In vivo –

>in the living individual.

Ionizing radiation –

>radiation sufficiently energetic to dislodge electrons from an atom.
>Ionizing radiation includes X and gamma radiation, electrons (beta
>radiation), alpha particles (helium nuclei), and heavier charged
>atomic nuclei. Neutrons ionize indirectly by colliding with atomic
>nuclei.

Kerma –

>Kinetic Energy Released in Material. A unit of exposure, expressed
>in rad, that represents the kinetic energy transferred to charged
>particles per unit mass of irradiated medium when indirectly ionizing
>(uncharged) particles, such as photons or neutrons, traverse the medium.

kVp –

>"kilovolt peak", a measure of the energy of the X-ray tube-voltage and
>hence of the maximum energy of the X-ray photons produced.

Latent period –

>also time to response, induction period; the period of seeming
>inactivity between the time of exposure of a tissue to an injurious
>agent (e.g., radiation) and observed response (e.g., diagnosis of
>cancer).

LET = linear energy transfer -

    a measure of ionization density of a given radiation. LET is the average loss in energy per unit length of path of the incident radiation. See high-LET and low-LET radiation.

Linear energy transfer

    see LET.

Life Span Study -

    see LSS.

Life Table -

    a table showing the number of persons who, of a given number born or living at a specified age, live to attain successive higher ages, together with the numbers who die in the intervals.

Linear (L) model -

    also, linear dose-effect relationship; expresses the effect (e.g., mutation or cancer) as a direct (linear) function of dose.

Linear-quadratic (LQ) model -

    also, linear-quadratic dose-effect relationship; expresses the effect (e.g., mutation or cancer) as partly directly proportional to the dose (linear term) and partly proportional to the square of the dose (quadratic term). The linear term will predominate at lower doses, the quadratic term at higher doses (see crossover dose).

Lognormal distribution -

    if the logarithms of a set of values are distributed according to a normal distribution they are said to have a lognormal distribution, or be distributed "lognormally."

Low-LET radiation -

    radiation producing low ionization density, such as X and gamma radiation, and accelerated electrons (see LET).

LSS -

    Life Span Study, refers to the study of a population of Japanese atomic-bomb survivors selected for lifetime follow-up study.

Millirad (mrad) -

    1/1000 of a "rad."

Millirem

1/1000 of a "rem."

Mortality (rate) –

the rate at which people die from a disease, e.g., a specific
type of cancer, often expressed as number of deaths per 100,000
per year.

Multiplicative interaction model (MIM) –

the assumption that the relative risk (= the relative excess risk
plus one) resulting from the exposure to two risk factors is the
product of the relative risks from the two factors taken separately.

NAS –

National Academy of Sciences.

NCRP –

National Council on Radiation Protection and Measurements.

Neutron –

uncharged subatomic particle capable of producing free radicals in
matter by indirect ionization.

Normal distribution –

a random variable X is said to be normally distributed if, for some
number μ and some positive number σ, $Y = (X - \mu)/\sigma$ has a standard
normal distribution with probability density function

$$\phi(y) = (2_\pi)^{-1/2} \exp(-y^2/2).$$

NRC –

National Research Council (in this report); a unit of the NAS.

PC = probability of causation –

a number that expresses the probability that a given cancer, in a
specific tissue, has been caused by a previous exposure to a carcinogenic
agent, such as radiation; essentially synonymous with "assigned share."

Probability of causation –

see PC.

Projection model –

a mathematical model that simultaneously describes the excess cancer

risk at different levels of some factor such as dose, time after exposure, or baseline level of risk, in terms of a parametric function of that factor. It becomes a projection model when data in a particular range of factor values are used to assign values to the parameters in order to estimate (or project) excess risk for factor values outside that range.

Promoter -

an agent which is not by itself carcinogenic, but which can amplify the effect of a true carcinogen by increasing the probability of late-stage cellular changes needed to complete the carcinogenic process.

Protraction -

the spreading out of a radiation dose over time by continuous delivery at a lower dose rate.

PY = person-years -

a unit used in epidemiological analyses, obtained by adding the numbers of years of observation for all members of the group studied. The number of PY may be used to predict the number of baseline cancers expected in the population group studied.

Quality factor -

also QF or Q, the LET-dependent factor by which absorbed doses are multiplied to obtain (for radiation protection purposes) a quantity that expresses the effectiveness of an absorbed dose on a common scale for all kinds of ionizing radiations. X rays at 250 kVp are usually used as reference radiation (Q = 1).

Rad -

unit of absorbed dose of ionizing radiation = 100 erg/g mass; a newer unit of absorbed radiation dose is the gray (Gy): 1 gray = 1 joule absorbed energy per kg mass; thus 1 gray = 100 rad. (Average background radiation in the U.S. is on the order of 0.1 - 0.2 rad annually.)

Radiation quality -

a general term referring to the spatial distribution of absorbed dose in extremely small volumes of target tissue. For example, an exposure to neutron radiation may be quantitatively the same as an exposure to gamma ray, in the sense that, for volumes of tissue on the order of one cubic centimeter, the absorbed energy is the same. Yet at resolutions of a few microns the ionizing events will be more uniformly dispersed for the gamma ray radiation than for the neutron radiation (see LET), producing quantitatively different biological effects (see (RBE).

Radiogenic -

   caused by radiation.

Radionuclide -

   a radioactive atomic species.

Radon daughters -

   (radioactive) decay products from the radioactive gas, radon (itself
   a decay product from radium).

RBE = relative biologic effectiveness -

   a factor used in comparing ionizing radiation of different types,
   generally by measuring the effectiveness relative to 250 kVp X radiation.
   For a given dose of given type of radiation, the RBE is the ratio of the
   dose of 250-kVp X rays to the dose of the given radiation that will pro-
   duce the same biological effect. For a given type of radiation, RBE
   varies with the energy, the magnitude of the dose, and with the end
   point studied.

Relative risk -

   an expression of excess risk relative to the underlying (baseline)
   risk; if the excess equals the baseline risk the relative risk is 2.

Rem -

   (rad equivalent, man); unit of dose equivalent. The dose equivalent
   in "rem" is numerically equal to the absorbed dose in "rad" multiplied
   by the "quality factor" (see this), the distribution factor and any
   other necessary modifying factor.

RERF -

   Radiation Effects Research Foundation; a Japanese foundation chartered
   by the Japanese Welfare Ministry under an agreement between the U.S.A
   and Japan. The RERF is the successor to the ABCC (Atomic Bomb Casualty
   Commission).

Risk coefficient -

   a fitted constant in an equation that describes how an effect depends
   on dose.

Sarcoma -

   a malignant growth arising in tissue of mesodermal origin (connective
   tissue, bone, cartilage or striated muscle).

SEER program -

Surveillance, Epidemiology and End Results, a nationwide system of
population-based cancer registries supported by the National Cancer
Institute to provide systematic cancer incidence data for the U.S.
Approximately 10 percent of the U.S. population is covered; data
for 1973-1977 are published, data are otherwise available through
1981. (The Working Group has used SEER data for base-line cancer
incidence rates in the present report.)

Stochastic -

a stochastic process is one in which the system incorporates an
element of randomness, as opposed to a deterministic system. As
used in this report (following ICRP), stochastic effects are those
in which the probability of an effect occurring rather than its
severity is a function of dose, without threshold.

Thorotrast -

a contrast agent used earlier (1928-1955) for X ray diagnostic
procedures; Thorotrast contains radioactive thorium-232 dioxide.

Threshold (dose) -

a specified level of dose below which, it is assumed, no radiation
injury of a specified type occurs.

Time-response model -

a mathematical model expressing the conditional probability
distribution of the time from exposure to a carcinogen until
diagnosis of a cancer caused by that exposure.

Tinea capitis -

ringworm of the scalp.

UNSCEAR -

United Nations Scientific Committee on the Effects of Atomic Radiation;
publishes periodic reports on sources and effects of ionizing radiation.

WL = Working Level -

any combination of short-lived radon daughters in one liter of air
that will result in the ultimate emission of 1.3×10^5 MeV of potential
alpha particle energy.

WLM = Working Level Month

exposure resulting from the inhalation of air with a concentration of
1 WL of radon daughter for 170 working hours. One WLM corresponds to
a dose of approximately 6 rem.

X radiation -

      also X rays; penetrating electromagnetic radiation, usually produced
      by bombarding a metallic target with fast electrons in a high vacuum.

Xeroderma pigmentosum (XP) -

      an inherited disease in which skin cells are highly susceptible
      to sun-induced cancer; XP cells have a defect in DNA repair after
      ultraviolet irradiation which apparently accounts for the propensity
      for this neoplasm.